L7 STRUCTURE UPLOADED

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FULL SEARCH INITIATED 19:49:36 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 155 TO ITERATE

100.0% PROCESSED 155 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

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=> s l8
L9 3 L8

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 2 DUP REM L9 (1 DUPLICATE REMOVED)

=> d ibib abs hitstr it 1-2

L10 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:703126 CAPLUS
DOCUMENT NUMBER: 141:200234
TITLE: Methods of treating conditions associated with the Edg-3 receptor
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004167181	A1	20040826	US 2004-760003		20040116
PRIORITY APPLN. INFO.:			US 2003-440322P	P	20030116

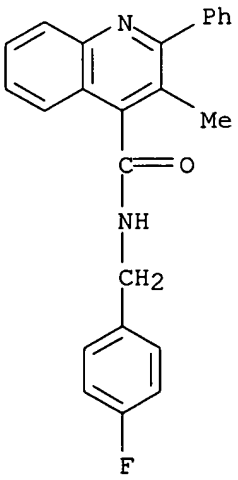
OTHER SOURCE(S): MARPAT 141:200234

AB The invention provides a method of inhibiting the Edg-3 receptor-mediated biol. activity in a cell. A cell expressing the Edg-3 receptor is contacted with an amount of an Edg-3 receptor inhibitor sufficient to inhibit the Edg-3 receptor-mediated biol. activity. Preferably, the inhibitor is not a phospholipid. Also the invention provides a method where an Edg-3 receptor-mediated biol. activity is inhibited in a subject. A therapeutically effective amount of an inhibitor of the Edg-3 receptor is administered to the subject. Preferably, the inhibitor is not a phospholipid.

IT **355000-90-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating conditions associated with Edg-3 receptor)

RN 355000-90-7 CAPLUS

CN 4-Quinolinecarboxamide, N-[(4-fluorophenyl)methyl]-3-methyl-2-phenyl- (9CI) (CA INDEX NAME)



IT Animal cell line
(A431; methods of treating conditions associated with Edg-3 receptor)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D2(long); methods of treating conditions associated with Edg-3 receptor)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG (endothelial differentiation gene); methods of treating conditions associated with Edg-3 receptor)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-1 (endothelial differentiation gene 1); methods of treating conditions associated with Edg-3 receptor)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-2 (endothelial differentiation gene 2); methods of treating conditions associated with Edg-3 receptor)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-3 (endothelial differentiation gene 3); methods of treating conditions associated with Edg-3 receptor)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-4 (endothelial differentiation gene 4); methods of treating

conditions associated with Edg-3 receptor)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-5 (endothelial differentiation gene 5); methods of treating conditions associated with Edg-3 receptor)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-6 (endothelial differentiation gene 6); methods of treating conditions associated with Edg-3 receptor)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-7 (endothelial differentiation gene 7); methods of treating conditions associated with Edg-3 receptor)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-8 (endothelial differentiation gene 8); methods of treating conditions associated with Edg-3 receptor)
IT Animal cell line
(HT-1080; methods of treating conditions associated with Edg-3 receptor)
IT Animal cell line
(HTC; methods of treating conditions associated with Edg-3 receptor)
IT Calcium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(L-type, dihydropyridine-sensitive; methods of treating conditions associated with Edg-3 receptor)
IT Animal cell line
(MDA-MB-231; methods of treating conditions associated with Edg-3 receptor)
IT Lung, disease
(acute; methods of treating conditions associated with Edg-3 receptor)
IT Respiratory distress syndrome
(adult; methods of treating conditions associated with Edg-3 receptor)
IT Antiarteriosclerotics
(antiatherosclerotics; methods of treating conditions associated with Edg-3 receptor)
IT Immunity
(autoimmunity; methods of treating conditions associated with Edg-3 receptor)
IT Uterus, neoplasm
(cervix; methods of treating conditions associated with Edg-3 receptor)
IT Lung, disease
(chronic, acute inflammatory exacerbation of; methods of treating conditions associated with Edg-3 receptor)
IT Intestine, neoplasm
(colorectal; methods of treating conditions associated with Edg-3 receptor)
IT Uterus, neoplasm
(endometrium; methods of treating conditions associated with Edg-3 receptor)
IT Sarcoma
(fibrosarcoma; methods of treating conditions associated with Edg-3 receptor)
IT Carcinoma
(hepatocellular; methods of treating conditions associated with Edg-3 receptor)
IT Liver, neoplasm
(hepatoma; methods of treating conditions associated with Edg-3 receptor)
IT Angiogenesis
Angiogenesis inhibitors
Anti-inflammatory agents
Anti-ischemic agents
Antiasthmatics
Antitumor agents

Apoptosis
Asthma
Atherosclerosis
Autoimmune disease
Burn
Carcinoma
Cardiovascular agents
Cardiovascular system, disease
Cell migration
Cell proliferation
Fibroblast
Human
Hydrolysis
Inflammation
Ischemia
Kidney, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Myoblast
Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Peritoneum, neoplasm
Pheochromocytoma
Platelet (blood)
Platelet activation
Platelet activation
Prostate gland, neoplasm
Stomach, neoplasm
Thyroid gland, neoplasm
Uterus, neoplasm
Wound healing
Wound healing promoters
(methods of treating conditions associated with Edg-3 receptor)

IT Actins
Calcium channel
Carbohydrates, biological studies
Interleukin 8
Ion channel
Muscarinic receptors
Nucleic acids
Phosphatidylinositols
Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods of treating conditions associated with Edg-3 receptor)

IT Intestine, neoplasm
(small; methods of treating conditions associated with Edg-3 receptor)

IT Injury
(surface epithelial cell; methods of treating conditions associated with Edg-3 receptor)

IT Freezing
(trans-corneal; methods of treating conditions associated with Edg-3 receptor)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT1; methods of treating conditions associated with Edg-3 receptor)

IT Angiotensin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type AT2; methods of treating conditions associated with Edg-3 receptor)

IT Endothelin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type ETA; methods of treating conditions associated with Edg-3 receptor)

IT 26993-30-6, Sphingosine-1-phosphate
RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(methods of treating conditions associated with Edg-3 receptor)
IT 60-92-4, CAMP 7440-70-2, Calcium, biological studies 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods of treating conditions associated with Edg-3 receptor)
IT 742058-66-8P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of treating conditions associated with Edg-3 receptor)
IT 177360-28-0 332161-39-4 346699-98-7 **355000-90-7**
389079-78-1 569656-28-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating conditions associated with Edg-3 receptor)
IT 4506-71-2 68984-05-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(methods of treating conditions associated with Edg-3 receptor)

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:591307 CAPLUS
DOCUMENT NUMBER: 139:143997
TITLE: Methods using Edg receptor modulators for the treatment of Edg receptor-associated conditions
INVENTOR(S): Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): Ceretek LLC, USA
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003062392	A2	20030731	WO 2003-US1881		20030121
WO 2003062392	A3	20050120			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2473740	AA	20030731	CA 2003-2473740		20030121
AU 2003214873	A1	20030902	AU 2003-214873		20030121
EP 1513522	A2	20050316	EP 2003-710713		20030121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005519915	T2	20050707	JP 2003-562260		20030121
US 2005261298	A1	20051124	US 2003-390428		20030314
PRIORITY APPLN. INFO.:			US 2002-350445P	P	20020118
			US 2002-350446P	P	20020118
			US 2002-350447P	P	20020118
			US 2002-350448P	P	20020118
			WO 2003-US1881	W	20030121

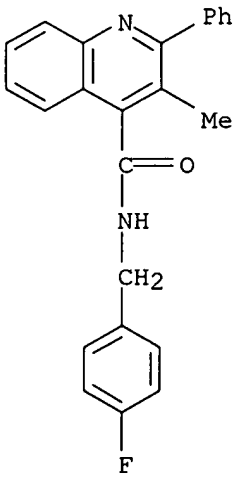
OTHER SOURCE(S): MARPAT 139:143997

AB The invention provides a method of modulating an Edg-2, Edg-3, Ed-4 or Edg7 receptor-mediated biol. activity in a cell. A cell expressing the Edg-2, Edg-3, Edg-4 or Edg 7 receptor is contacted with a modulator of the Edg-2, Edg-3, Ed-4 or Edg 7 receptor sufficient to modulate receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-2, Edg-3, Ed-4 or Edg-7 receptor mediated biol. in a subject. A therapeutically effective amount of a modulator of the Edg-2, Edg-3, Ed-4 or Edg7 receptor is administered to the subject. Preparation of compds., e.g. 4,4,4-trifluoro-3-oxo-N-(5-phenyl-2H-pyrazol-3-yl)butyramide, is described.

IT **355000-90-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

RN 355000-90-7 CAPLUS

CN 4-Quinolinecarboxamide, N-[(4-fluorophenyl)methyl]-3-methyl-2-phenyl- (9CI) (CA INDEX NAME)



IT Animal cell line
(A431; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(CAOV-3; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Inflammation
(Crohn's disease; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Intestine, disease
(Crohn's; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-1 (endothelial differentiation gene 1); Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-2 (endothelial differentiation gene 2); Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-3 (endothelial differentiation gene 3); Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-5 (endothelial differentiation gene 5); Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-6 (endothelial differentiation gene 6); Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT G protein-coupled receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EDG-8 (endothelial differentiation gene 8); Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Angiogenesis
Angiogenesis inhibitors
Anti-inflammatory agents
Anti-ischemic agents
Antiasthmatics
Antimigraine agents
Antirheumatic agents
Antitumor agents
Apoptosis
Asthma
Atherosclerosis
Behcet's syndrome
Cardiovascular agents
Cardiovascular system, disease
Cell migration
Cell proliferation
Cytotoxic agents
Fibroblast
Gastrointestinal agents
Human
Inflammation
Ischemia
Kidney, neoplasm
Lung, disease
Lung, neoplasm
Mammary gland, neoplasm
Neoplasm
Neuron
Ovary, neoplasm
Pancreas, neoplasm
Peritoneum, neoplasm
Platelet (blood)
Platelet activation
Platelet activation
Prostate gland, neoplasm
Psoriasis
Rheumatoid arthritis
Stomach, neoplasm
Thyroid gland, neoplasm
Uterus, neoplasm
Vasoconstriction
Vasodilators
Wound
Wound healing promoters
(Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Carbohydrates, biological studies

Nucleic acids
Organic compounds, biological studies
Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Edg-4; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Edg-7; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Edg; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(HT-1080; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(HTC; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(HUVEC; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Chemotaxis
(LPA-stimulated; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(MDA-MB-231; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(MDA-MB-453; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(OV202; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Animal cell line
(SKOV3; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Respiratory distress syndrome
(adult; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Antiarteriosclerotics
(antiatherosclerotics; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Anemia (disease)
Autoimmune disease
(autoimmune hemolytic anemia; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Immunity
(autoimmunity; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Lysophosphatidic acids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cell proliferation stimulated by; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Carcinoma
Myoblast
Pheochromocytoma

(cell; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Artery
(cerebral, vasoconstriction; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Uterus, neoplasm
(cervix; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Resolution (separation)
(chromatog.; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Infection
(chronic active hepatitis; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Inflammation
Kidney, disease
(chronic glomerulonephritis; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Temperature effects, biological
(cold, transcomeal freezing; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Intestine, neoplasm
(colon; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Intestine, neoplasm
(colorectal; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Burn
(cutaneous; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Meninges
(disease, subarachnoid hemorrhage; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Uterus, neoplasm
(endometrium; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Blood vessel
(endothelium; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Epithelium
(epithelial cell; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Carcinoma
(epithelioid; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Sarcoma
(fibrosarcoma, cell; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Carcinoma
(hepatocellular; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Liver, neoplasm
(hepatoma; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Phosphatidylinositols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrolysis; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(level of; Edg receptor modulators for treatment of Edg receptor-associated conditions)
IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lysophosphatidic acid; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Neoplasm
(metastasis; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Headache
(migraine; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Kidney, disease
(non-glomerular nephrosis; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Blood vessel, disease
(occlusion; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Egg
(oocyte, Xenopus laevis; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Xenopus laevis
(oocyte; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Ovary
(ovarian cell; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Actins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polymerization; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Intestine, neoplasm
(small; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Blood vessel, disease
(spasm; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Brain, disease
(stroke; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Hemorrhage
(subarachnoid; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Injury
(surface epithelial cell; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Interleukin 8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Lupus erythematosus
(systemic; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Purpura (disease)
(thrombocytopenic, chronic; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Inflammation
Intestine, disease
(ulcerative colitis; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Endothelium
(vascular; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT Hepatitis
(viral, chronic active; Edg receptor modulators for treatment of Edg

receptor-associated conditions)

IT 182762-25-0, GenBank X83864 218763-60-1, GenBank AJ000479 259476-69-2, GenBank AF233092 262400-57-7, GenBank AF233090 384729-36-6, GenBank U78192 385223-15-4, GenBank AF011466 390105-18-7, GenBank AF034780 390174-36-4, GenBank AF233365 390523-03-2, GenBank AF317676 392101-34-7, GenBank AF127138
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 473390-98-6
RL: FMU (Formation, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 353273-74-2P 569655-94-3P 569655-95-4P 569655-96-5P 569656-23-1P 569656-24-2P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 94835-69-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 7741-53-9P 40622-01-3P 173275-26-8P 304650-31-5P 311799-07-2P 312501-62-5P 312519-16-7P 331945-22-3P 334498-72-5P 342384-25-2P 353253-35-7P 353771-45-6P **355000-90-7P** 569656-08-2P 569656-09-3P 569656-10-6P 569656-11-7P 569656-12-8P 569656-13-9P 569656-14-0P 569656-15-1P 569656-16-2P 569656-17-3P 569656-18-4P 569656-19-5P 569656-20-8P 569656-21-9P 569656-25-3P 569656-26-4P 569656-27-5P 569656-29-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 49843-94-9 90212-73-0 107235-67-6 136382-28-0 171286-07-0 177360-28-0 292076-38-1 306764-68-1 309282-30-2 311773-65-6 312594-43-7 321679-76-9 322662-05-5 327167-87-3 329350-38-1 330630-42-7 331274-84-1 332161-39-4 337349-59-4 337469-26-8 337498-14-3 346699-98-7 353463-50-0 353793-15-4 364051-15-0 383164-60-1 389079-78-1 400064-03-1 569655-97-6 569655-98-7 569656-22-0 569656-28-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 50-30-6, 2,6-Dichlorobenzoic acid 50-45-3, 2,3-Dichlorobenzoic acid 70-11-1, 2-Bromoacetophenone 79-19-6, Thiosemicarbazide 83-38-5, 2,6-Dichlorobenzaldehyde 91-56-5, 1H-Indole-2,3-dione 93-17-4, 3,4-Dimethoxyphenylacetonitrile 93-55-0, Propiophenone 98-59-9, p-Toluenesulfonyl chloride 98-88-4, Benzoyl chloride 98-95-3, Nitrobenzene, reactions 100-65-2, N-Phenylhydroxylamine 108-31-6, Maleic anhydride, reactions 108-38-3, 1,3-Dimethylbenzene, reactions 120-72-9, Indole, reactions 123-11-5, p-Anisaldehyde, reactions 140-75-0, 4-Fluorobenzylamine 302-01-2, Hydrazine, reactions 363-58-6 372-31-6, Ethyl 4,4,4-trifluoroacetoacetate 406-00-8, 4-Fluorophenylhydroxylamine 434-75-3, 2-Chloro-6-fluorobenzoic acid

'533-18-6, o-Tolyl acetate 556-90-1, Pseudothiohydantoin 619-05-6, 3,4-Diaminobenzoic acid 619-41-0, 2-Bromo-4'-methylacetophenone 829-20-9 1226-42-2, 4,4'-Dimethoxybenzil 1468-83-3, 3-Acetylthiophene 1476-23-9, Allyl isocyanate 1572-10-7 2642-63-9, 3',4'-Dichloroacetophenone 4506-71-2 5242-26-2 5351-85-9 6629-60-3, Ethylhydrazine oxalate 13100-05-5 13380-67-1 19541-95-8 23448-86-4 23821-37-6 36817-57-9 39151-19-4 64900-65-8, 2-Chlorobenzenesulfonyl isocyanate 72411-52-0 82799-44-8 89570-85-4 96799-03-0 96799-04-1 569656-04-8 569656-05-9 569656-06-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 5351-91-7P 5467-70-9P 6292-74-6P 7420-34-0P 7741-54-0P 43071-45-0P 76293-13-5P 82799-45-9P 86358-85-2P 91912-53-7P 112612-58-5P 113054-02-7P 149246-80-0P 149246-86-6P 208519-10-2P 208519-15-7P 329069-72-9P 502132-61-8P 569655-99-8P 569656-00-4P 569656-01-5P 569656-02-6P 569656-03-7P 569656-07-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 26993-30-6, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium mobilization stimulated by; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 60-92-4, Cyclic AMP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(formation inhibition; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mobilization; Edg receptor modulators for treatment of Edg receptor-associated conditions)

IT 127464-60-2, Vascular endothelial growth factor

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             6 182762-25-0/BI
            49 19541-95-8/BI
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            15 218763-60-1/BI
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L27        332 L26 AND EDG

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                 (EDG(W)E)
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=> s l26 and edg-3
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=> focus
PROCESSING COMPLETED FOR L30
L31          34 FOCUS L30 1-

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L31  ANSWER 1 OF 34  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2003:591307  CAPLUS
DOCUMENT NUMBER:          139:143997
TITLE:                    Methods using Edg receptor modulators for the
                          treatment of Edg receptor-associated conditions
INVENTOR(S):              Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet
                          V.; Gluchowski, Charles
PATENT ASSIGNEE(S):       Ceretek LLC, USA
SOURCE:                   PCT Int. Appl., 293 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   4
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2003062392         A2    20030731    WO 2003-US1881          20030121
     WO 2003062392         A3    20050120
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
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             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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AU 2003214873	A1	20030902	AU 2003-214873		20030121
EP 1513522	A2	20050316	EP 2003-710713		20030121
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JP 2005519915	T2	20050707	JP 2003-562260		20030121
US 2005261298	A1	20051124	US 2003-390428		20030314
PRIORITY APPLN. INFO.:			US 2002-350445P	P	20020118
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			US 2002-350448P	P	20020118
			WO 2003-US1881	W	20030121
			US 2003-352579	B2	20030127

OTHER SOURCE(S): MARPAT 139:143997

AB The invention provides a method of modulating an Edg-2, **Edg-3**, Ed-4 or Edg7 receptor-mediated biol. activity in a cell. A cell expressing the Edg-2, **Edg-3**, Edg-4 or Edg 7 receptor is contacted with a modulator of the Edg-2, **Edg-3**, Ed-4 or Edg 7 receptor sufficient to modulate receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-2, **Edg-3**, Ed-4 or Edg-7 receptor mediated biol. in a subject. A therapeutically effective amount of a modulator of the Edg-2, **Edg-3**, Ed-4 or Edg7 receptor is administered to the subject. Preparation of compds., e.g. 4,4,4-trifluoro-3-oxo-N-(5-phenyl-2H-pyrazol-3-yl)butyramide, is described.

IT **182762-25-0**, GenBank X83864 **218763-60-1**, GenBank AJ000479 **259476-69-2**, GenBank AF233092 **262400-57-7**, GenBank AF233090 **384729-36-6**, GenBank U78192 **385223-15-4**, GenBank AF011466 **390105-18-7**, GenBank AF034780 **390174-36-4**, GenBank AF233365 **390523-03-2**, GenBank AF317676 **392101-34-7**, GenBank AF127138
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

RN 182762-25-0 CAPLUS
CN DNA (human gene EDG-3 plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 218763-60-1 CAPLUS
CN DNA (human dendritic cell gene EDG6 G protein-coupled receptor cDNA plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 259476-69-2 CAPLUS
CN DNA (human gene EDG4 lysophosphatidic acid receptor 4 cDNA plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 262400-57-7 CAPLUS
CN GenBank AF233090 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 384729-36-6 CAPLUS
CN GenBank U78192 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 385223-15-4 CAPLUS
CN GenBank AF011466 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 390105-18-7 CAPLUS

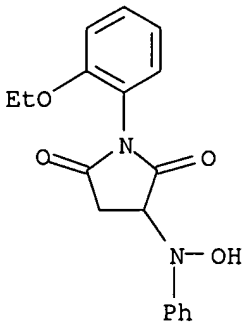
CN GenBank AF034780 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 390174-36-4 CAPLUS
CN DNA (human gene CHEDG1 cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 390523-03-2 CAPLUS
CN GenBank AF317676 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 392101-34-7 CAPLUS
CN GenBank AF127138 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **353273-74-2P 569655-94-3P 569655-95-4P**
569655-96-5P 569656-23-1P 569656-24-2P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)
RN 353273-74-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)- (9CI) (CA INDEX NAME)



RN 569655-94-3 CAPLUS
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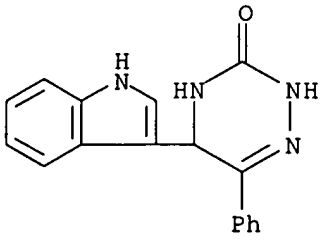
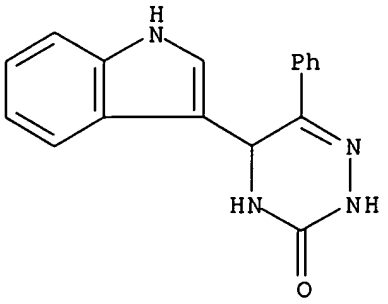


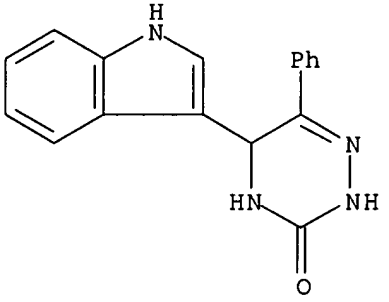
RN 569655-95-4 CAPLUS
CN 1,2,4-Triazin-3(2H)-one, 4,5-dihydro-5-(1H-indol-3-yl)-6-phenyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



RN 569655-96-5 CAPLUS
CN 1,2,4-Triazin-3(2H)-one, 4,5-dihydro-5-(1H-indol-3-yl)-6-phenyl-, (+)-
(9CI) (CA INDEX NAME)

Rotation (+).



RN 569656-23-1 CAPLUS
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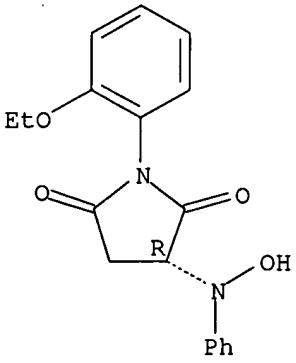
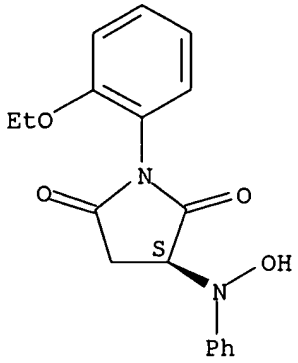
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 569656-24-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)-, (3S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **173275-26-8P 304650-31-5P 311799-07-2P**
312501-62-5P 312519-16-7P 331945-22-3P
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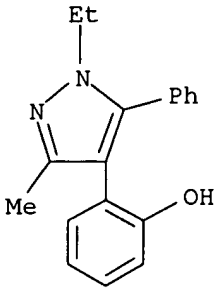
569656-12-8P 569656-13-9P 569656-14-0P
569656-15-1P 569656-16-2P 569656-17-3P
569656-18-4P 569656-19-5P 569656-20-8P
569656-21-9P 569656-25-3P 569656-26-4P
569656-27-5P 569656-29-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

RN 173275-26-8 CAPLUS
CN Phenol, 2-(1-ethyl-3-methyl-5-phenyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



RN 304650-31-5 CAPLUS
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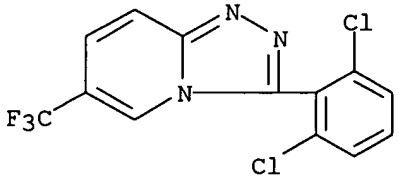
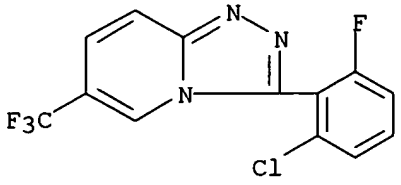


RN 311799-07-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyridine, 3-(2-chloro-6-fluorophenyl)-6-(trifluoromethyl)- (9CI) (CA INDEX NAME)



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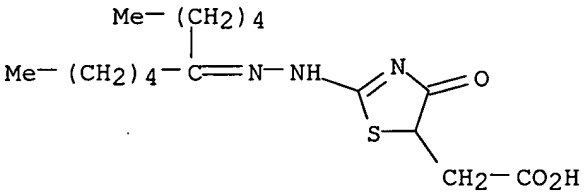
CN 5-Thiazoleacetic acid, 4,5-dihydro-4-oxo-2-[(1-pentylhexylidene)hydrazino]- (9CI) (CA INDEX NAME)



RN 312519-16-7 CAPLUS
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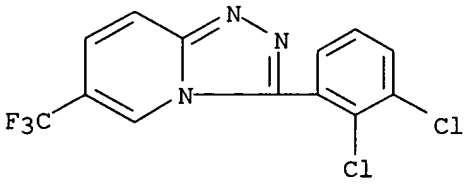
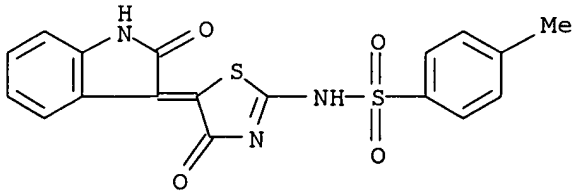


RN 331945-22-3 CAPLUS
CN Benzenesulfonamide, N-[5-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)-4,5-dihydro-4-oxo-2-thiazolyl]-4-methyl- (9CI) (CA INDEX NAME)



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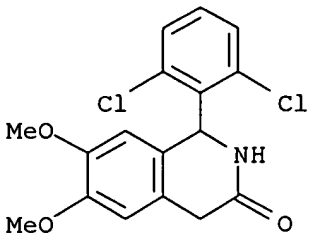
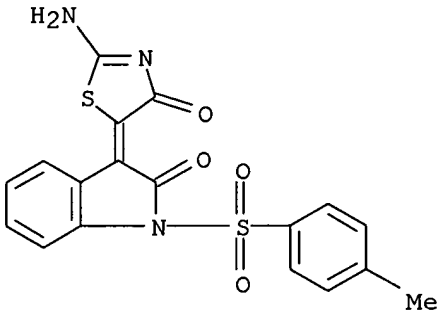
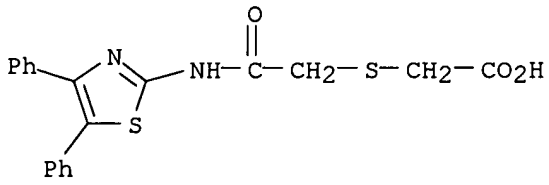


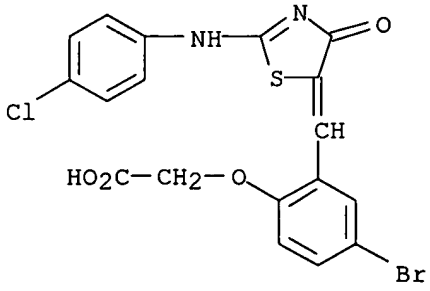
RN 342384-25-2 CAPLUS
CN 2H-Indol-2-one, 3-(2-amino-4-oxo-5(4H)-thiazolylidene)-1,3-dihydro-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



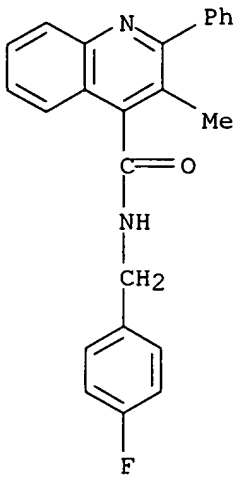
RN 353253-35-7 CAPLUS
CN Acetic acid, [[2-[(4,5-diphenyl-2-thiazolyl)amino]-2-oxoethyl]thio]- (9CI) (CA INDEX NAME)



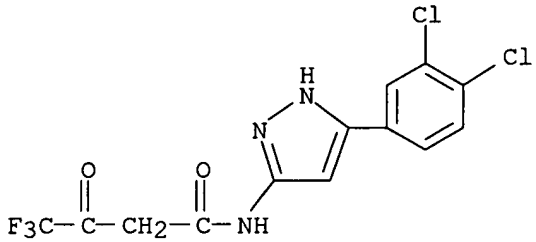
RN 353771-45-6 CAPLUS
CN Acetic acid, [4-bromo-2-[[2-[(4-chlorophenyl)amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenoxy]- (9CI) (CA INDEX NAME)



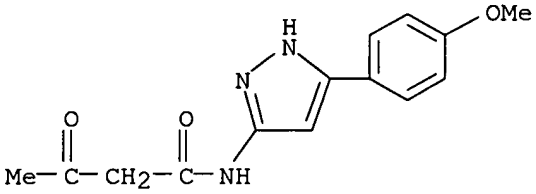
RN 355000-90-7 CAPLUS
CN 4-Quinolinecarboxamide, N-[(4-fluorophenyl)methyl]-3-methyl-2-phenyl- (9CI) (CA INDEX NAME)



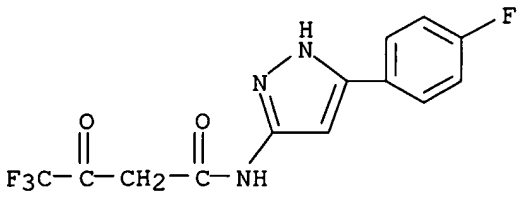
RN 569656-08-2 CAPLUS
CN Butanamide, N-[5-(3,4-dichlorophenyl)-1H-pyrazol-3-yl]-4,4,4-trifluoro-3-oxo- (9CI) (CA INDEX NAME)



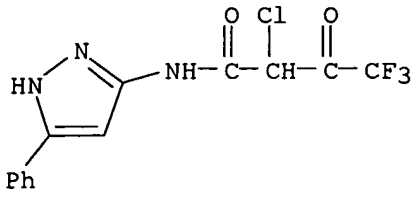
RN 569656-09-3 CAPLUS
CN Butanamide, N-[5-(4-methoxyphenyl)-1H-pyrazol-3-yl]-3-oxo- (9CI) (CA INDEX NAME)



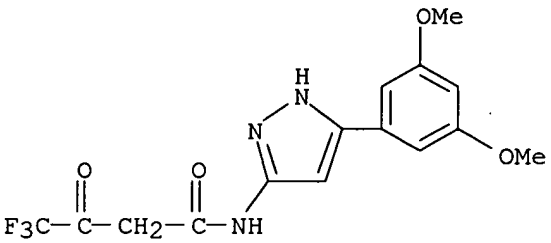
RN 569656-10-6 CAPLUS
CN Butanamide, 4,4,4-trifluoro-N-[5-(4-fluorophenyl)-1H-pyrazol-3-yl]-3-oxo- (9CI) (CA INDEX NAME)



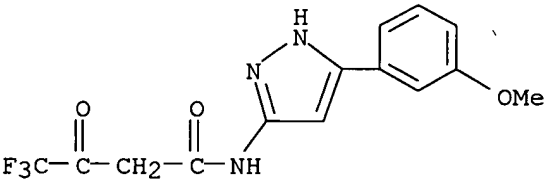
RN 569656-11-7 CAPLUS
CN Butanamide, 2-chloro-4,4,4-trifluoro-3-oxo-N-(5-phenyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



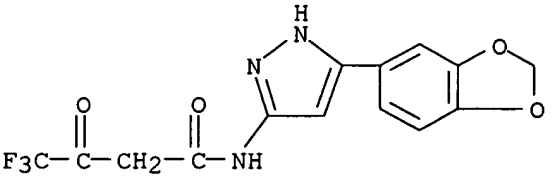
RN 569656-12-8 CAPLUS
CN Butanamide, N-[5-(3,5-dimethoxyphenyl)-1H-pyrazol-3-yl]-4,4,4-trifluoro-3-oxo- (9CI) (CA INDEX NAME)



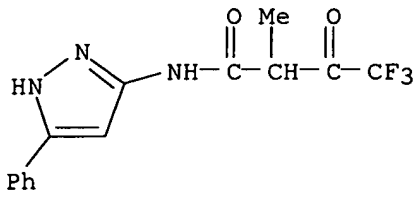
RN 569656-13-9 CAPLUS
CN Butanamide, 4,4,4-trifluoro-N-[5-(3-methoxyphenyl)-1H-pyrazol-3-yl]-3-oxo-(9CI) (CA INDEX NAME)



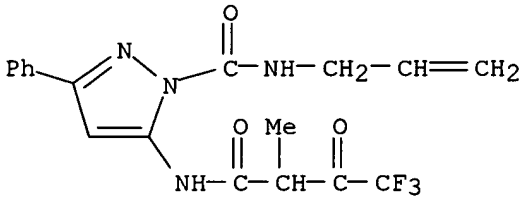
RN 569656-14-0 CAPLUS
CN Butanamide, N-[5-(1,3-benzodioxol-5-yl)-1H-pyrazol-3-yl]-4,4,4-trifluoro-3-oxo- (9CI) (CA INDEX NAME)



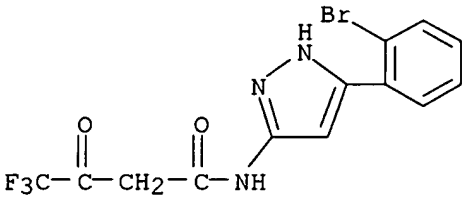
RN 569656-15-1 CAPLUS
CN Butanamide, 4,4,4-trifluoro-2-methyl-3-oxo-N-(5-phenyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



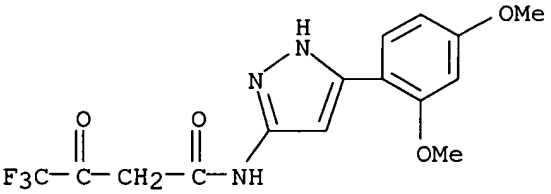
RN 569656-16-2 CAPLUS
CN 1H-Pyrazole-1-carboxamide, 3-phenyl-N-2-propenyl-5-[(4,4,4-trifluoro-2-methyl-1,3-dioxobutyl)amino]- (9CI) (CA INDEX NAME)



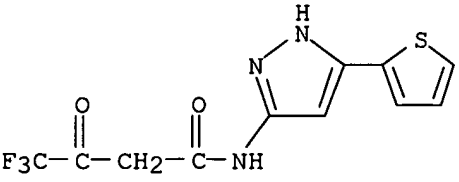
RN 569656-17-3 CAPLUS
CN Butanamide, N-[5-(2-bromophenyl)-1H-pyrazol-3-yl]-4,4,4-trifluoro-3-oxo- (9CI) (CA INDEX NAME)



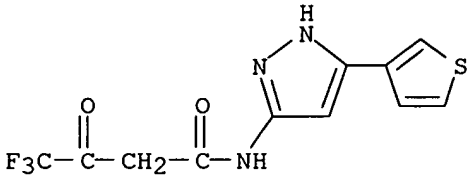
RN 569656-18-4 CAPLUS
CN Butanamide, N-[5-(2,4-dimethoxyphenyl)-1H-pyrazol-3-yl]-4,4,4-trifluoro-3-oxo- (9CI) (CA INDEX NAME)



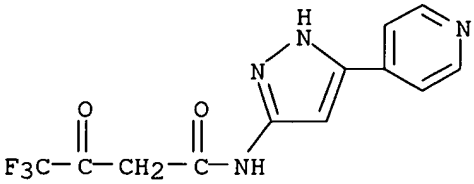
RN 569656-19-5 CAPLUS
CN Butanamide, 4,4,4-trifluoro-3-oxo-N-[5-(2-thienyl)-1H-pyrazol-3-yl]- (9CI) (CA INDEX NAME)



RN 569656-20-8 CAPLUS
CN Butanamide, 4,4,4-trifluoro-3-oxo-N-[5-(3-thienyl)-1H-pyrazol-3-yl]- (9CI) (CA INDEX NAME)

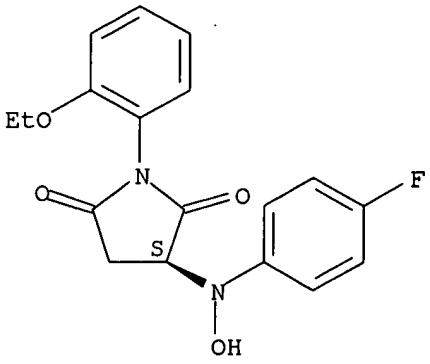


RN 569656-21-9 CAPLUS
CN Butanamide, 4,4,4-trifluoro-3-oxo-N-[5-(4-pyridinyl)-1H-pyrazol-3-yl]- (9CI) (CA INDEX NAME)



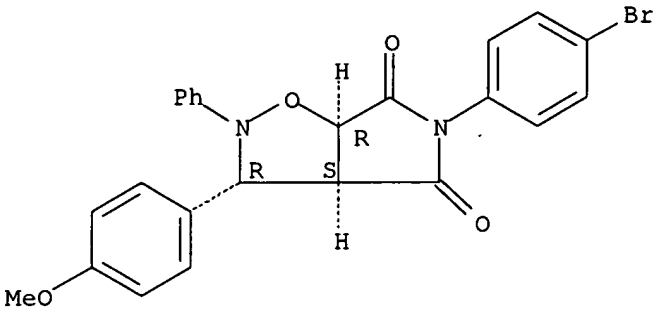
RN 569656-25-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-[(4-fluorophenyl)hydroxyamino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



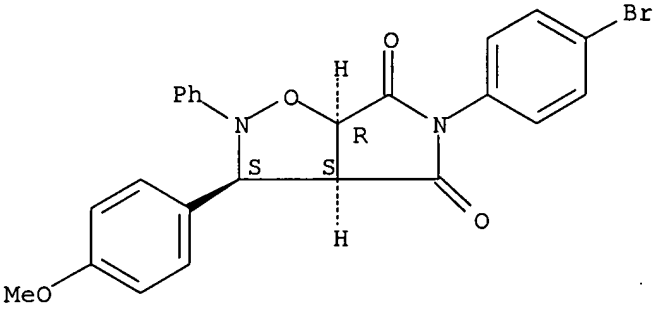
RN 569656-26-4 CAPLUS
CN 2H-Pyrrolo[3,4-d]isoxazole-4,6(3H,5H)-dione, 5-(4-bromophenyl)dihydro-3-(4-methoxyphenyl)-2-phenyl-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

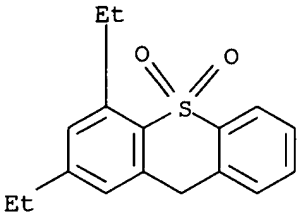


RN 569656-27-5 CAPLUS
CN 2H-Pyrrolo[3,4-d]isoxazole-4,6(3H,5H)-dione, 5-(4-bromophenyl)dihydro-3-(4-methoxyphenyl)-2-phenyl-, (3S,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

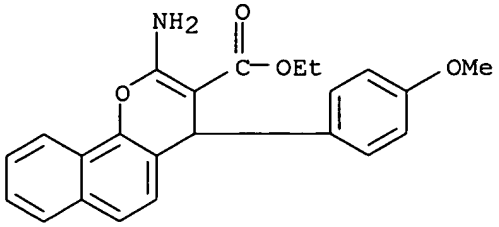


RN 569656-29-7 CAPLUS
CN 9H-Thioxanthene, 2,4-diethyl-, 10,10-dioxide (9CI) (CA INDEX NAME)

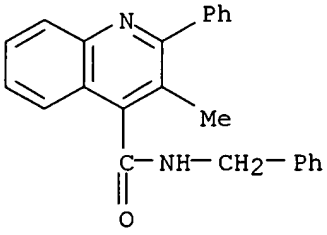


IT **171286-07-0 177360-28-0 292076-38-1**
306764-68-1 309282-30-2 311773-65-6
312594-43-7 321679-76-9 322662-05-5
327167-87-3 329350-38-1 330630-42-7
331274-84-1 332161-39-4 337349-59-4
337469-26-8 337498-14-3 346699-98-7
353463-50-0 353793-15-4 383164-60-1
389079-78-1 400064-03-1 569655-97-6
569655-98-7 569656-22-0 569656-28-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

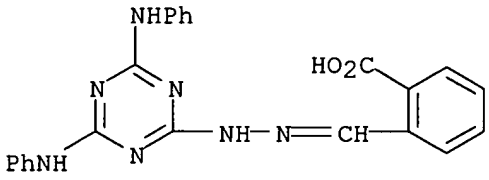
RN 171286-07-0 CAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carboxylic acid, 2-amino-4-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)



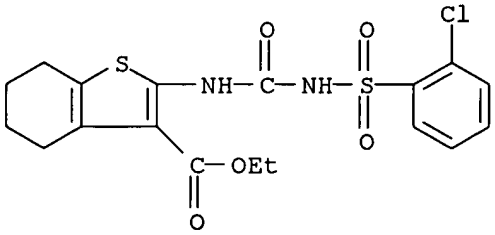
RN 177360-28-0 CAPLUS
CN 4-Quinolinecarboxamide, 3-methyl-2-phenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



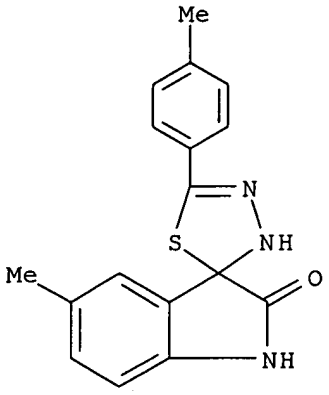
RN 292076-38-1 CAPLUS
CN Benzoic acid, 2-[[[4,6-bis(phenylamino)-1,3,5-triazin-2-yl]hydrazono]methyl]- (9CI) (CA INDEX NAME)



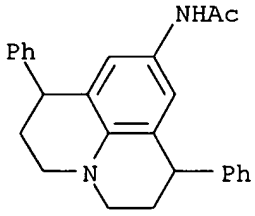
RN 306764-68-1 CAPLUS
CN Benzo[b]thiophene-3-carboxylic acid, 2-[[[[(2-chlorophenyl)sulfonyl]amino]carbonyl]amino]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)



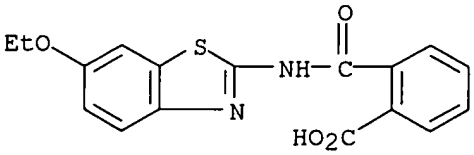
RN 309282-30-2 CAPLUS
CN Spiro[3H-indole-3,2'(3'H)-[1,3,4]thiadiazol]-2(1H)-one, 5-methyl-5'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



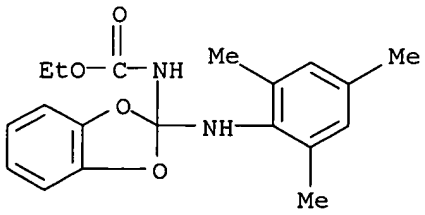
RN 311773-65-6 CAPLUS
CN Acetamide, N-(1,7-diphenyl-2,3,6,7-tetrahydro-1H,5H-benzo[ij]quinolizin-9-yl)- (9CI) (CA INDEX NAME)



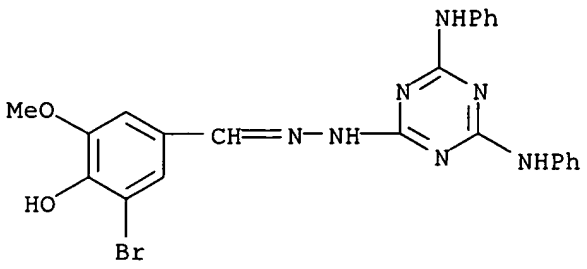
RN 312594-43-7 CAPLUS
CN Benzoic acid, 2-[[(6-ethoxy-2-benzothiazolyl)amino]carbonyl]- (9CI) (CA INDEX NAME)



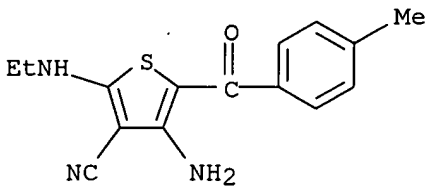
RN 321679-76-9 CAPLUS
CN Carbamic acid, [2-[(2,4,6-trimethylphenyl)amino]-1,3-benzodioxol-2-yl]-, ethyl ester (9CI) (CA INDEX NAME)



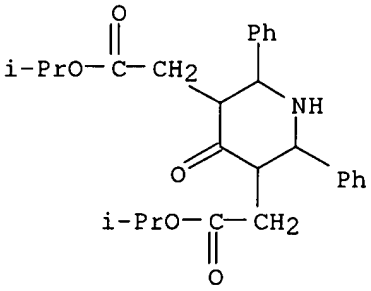
RN 322662-05-5 CAPLUS
CN Benzaldehyde, 3-bromo-4-hydroxy-5-methoxy-, [4,6-bis(phenylamino)-1,3,5-triazin-2-yl]hydrazone (9CI) (CA INDEX NAME)



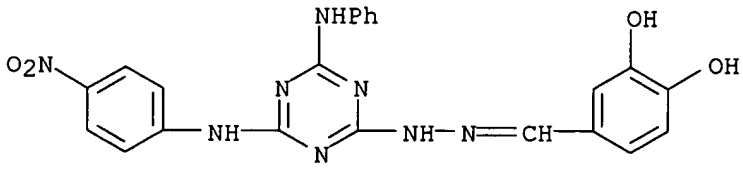
RN 327167-87-3 CAPLUS
CN 3-Thiophenecarbonitrile, 4-amino-2-(ethylamino)-5-(4-methylbenzoyl)- (9CI) (CA INDEX NAME)



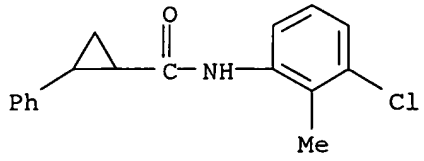
RN 329350-38-1 CAPLUS
CN 3,5-Piperidinediacetic acid, 4-oxo-2,6-diphenyl-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



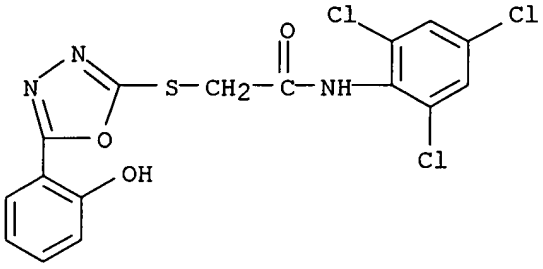
RN 330630-42-7 CAPLUS
CN Benzaldehyde, 3,4-dihydroxy-, [4-[(4-nitrophenyl)amino]-6-(phenylamino)-1,3,5-triazin-2-yl]hydrazone (9CI) (CA INDEX NAME)



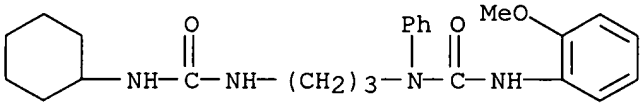
RN 331274-84-1 CAPLUS
CN Cyclopropanecarboxamide, N-(3-chloro-2-methylphenyl)-2-phenyl- (9CI) (CA INDEX NAME)



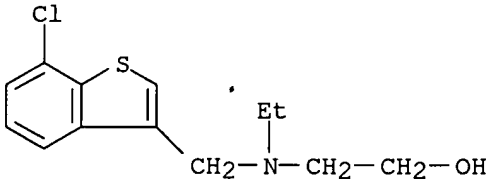
RN 332161-39-4 CAPLUS
CN Acetamide, 2-[[5-(2-hydroxyphenyl)-1,3,4-oxadiazol-2-yl]thio]-N-(2,4,6-trichlorophenyl)- (9CI) (CA INDEX NAME)



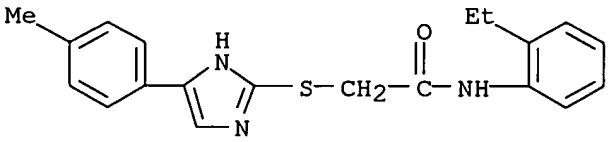
RN 337349-59-4 CAPLUS
CN Urea, N-[3-[[(cyclohexylamino)carbonyl]amino]propyl]-N'-(2-methoxyphenyl)-N-phenyl- (9CI) (CA INDEX NAME)



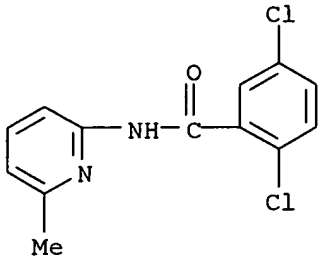
RN 337469-26-8 CAPLUS
CN Ethanol, 2-[[(7-chlorobenzo[b]thien-3-yl)methyl]ethylamino]- (9CI) (CA INDEX NAME)



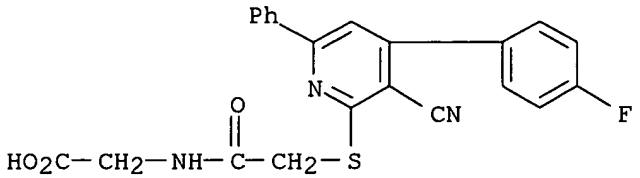
RN 337498-14-3 CAPLUS
CN Acetamide, N-(2-ethylphenyl)-2-[[4-(4-methylphenyl)-1H-imidazol-2-yl]thio]- (9CI) (CA INDEX NAME)



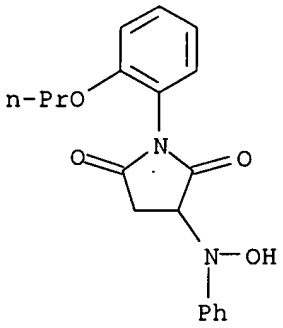
RN 346699-98-7 CAPLUS
CN Benzamide, 2,5-dichloro-N-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)



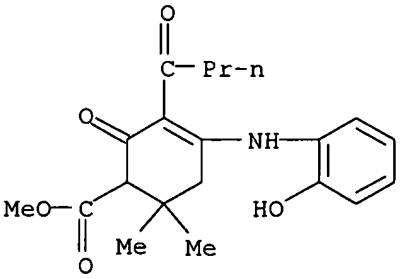
RN 353463-50-0 CAPLUS
CN Glycine, N-[[[3-cyano-4-(4-fluorophenyl)-6-phenyl-2-pyridinyl]thio]acetyl]- (9CI) (CA INDEX NAME)



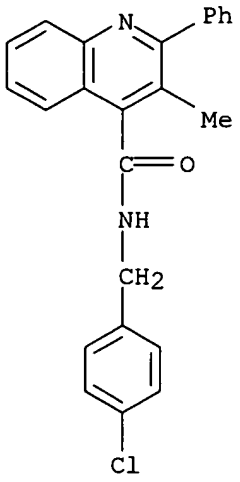
RN 353793-15-4 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(hydroxyphenylamino)-1-(2-propoxyphenyl)- (9CI) (CA INDEX NAME)



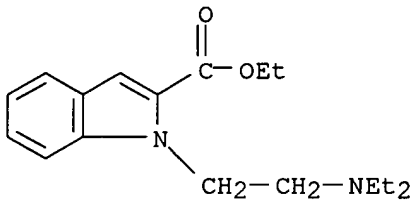
RN 383164-60-1 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 4-[(2-hydroxyphenyl)amino]-6,6-dimethyl-2-oxo-3-(1-oxobutyl)-, methyl ester (9CI) (CA INDEX NAME)



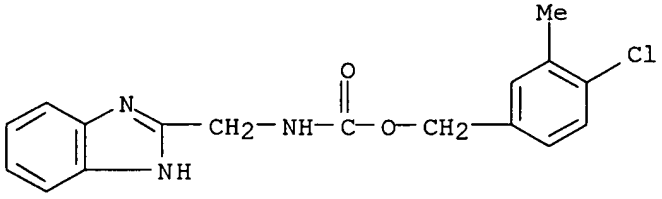
RN 389079-78-1 CAPLUS
CN 4-Quinolinecarboxamide, N-[(4-chlorophenyl)methyl]-3-methyl-2-phenyl- (9CI) (CA INDEX NAME)



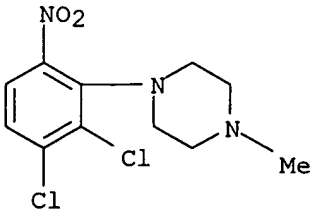
RN 400064-03-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-(diethylamino)ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



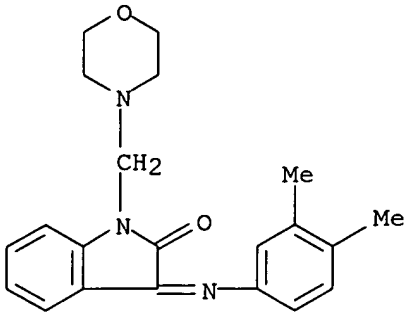
RN 569655-97-6 CAPLUS
CN Carbamic acid, (1H-benzimidazol-2-ylmethyl)-, (4-chloro-3-methylphenyl)methyl ester (9CI) (CA INDEX NAME)



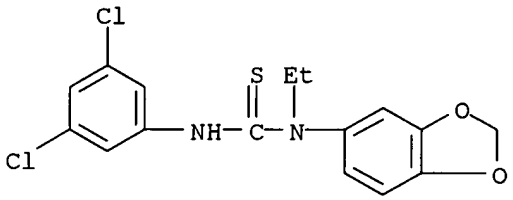
RN 569655-98-7 CAPLUS
CN Piperazine, 1-(2,3-dichloro-6-nitrophenyl)-4-methyl- (9CI) (CA INDEX NAME)



RN 569656-22-0 CAPLUS
CN 2H-Indol-2-one, 3-[(3,4-dimethylphenyl)imino]-1,3-dihydro-1-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)

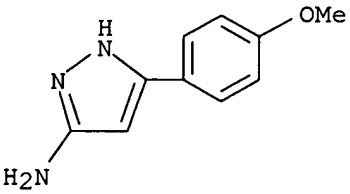


RN 569656-28-6 CAPLUS
CN Thiourea, N-1,3-benzodioxol-5-yl-N'-(3,5-dichlorophenyl)-N-ethyl- (9CI) (CA INDEX NAME)

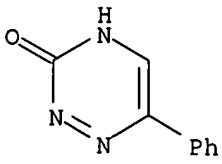


IT **19541-95-8 23448-86-4 23821-37-6 39151-19-4 569656-04-8 569656-05-9 569656-06-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

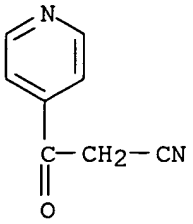
RN 19541-95-8 CAPLUS
CN 1H-Pyrazol-3-amine, 5-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)



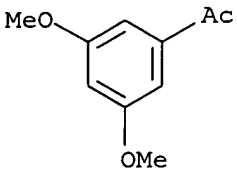
RN 23448-86-4 CAPLUS
CN 1,2,4-Triazin-3(2H)-one, 6-phenyl- (9CI) (CA INDEX NAME)



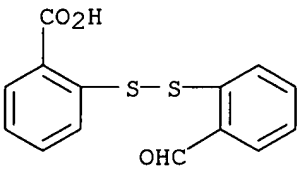
RN 23821-37-6 CAPLUS
CN 4-Pyridinepropanenitrile, β-oxo- (9CI) (CA INDEX NAME)



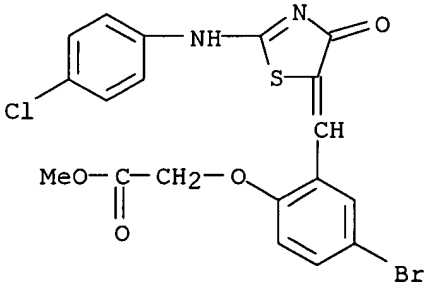
RN 39151-19-4 CAPLUS
CN Ethanone, 1-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



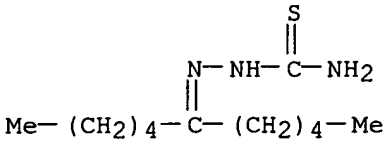
RN 569656-04-8 CAPLUS
CN Benzoic acid, 2-[(2-formylphenyl)dithio]- (9CI) (CA INDEX NAME)



RN 569656-05-9 CAPLUS
CN Acetic acid, [4-bromo-2-[[2-[(4-chlorophenyl)amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)

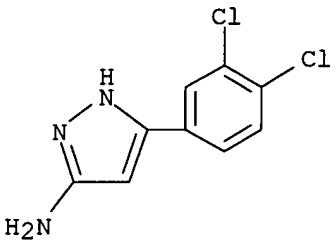


RN 569656-06-0 CAPLUS
CN Hydrazinecarbothioamide, 2-(1-pentylhexylidene)- (9CI) (CA INDEX NAME)

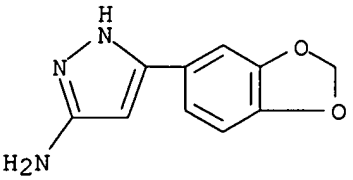


IT **208519-10-2P 208519-15-7P 329069-72-9P**
569655-99-8P 569656-00-4P 569656-01-5P
569656-02-6P 569656-03-7P 569656-07-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Edg receptor modulators for treatment of Edg receptor-associated conditions)

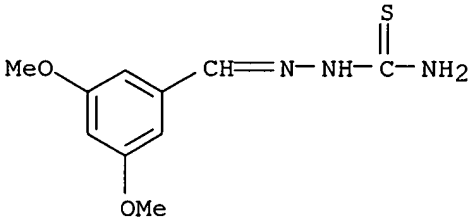
RN 208519-10-2 CAPLUS
CN 1H-Pyrazol-3-amine, 5-(3,4-dichlorophenyl)- (9CI) (CA INDEX NAME)



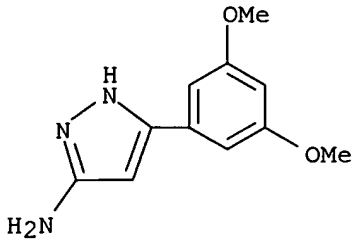
RN 208519-15-7 CAPLUS
CN 1H-Pyrazol-3-amine, 5-(1,3-benzodioxol-5-yl)- (9CI) (CA INDEX NAME)



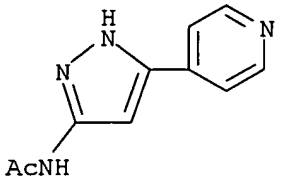
RN 329069-72-9 CAPLUS
CN Hydrazinecarbothioamide, 2-[(3,5-dimethoxyphenyl)methylene]- (9CI) (CA INDEX NAME)



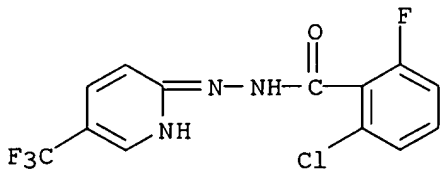
RN 569655-99-8 CAPLUS
CN 1H-Pyrazol-3-amine, 5-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



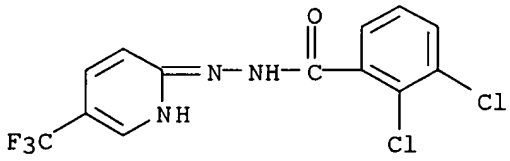
RN 569656-00-4 CAPLUS
CN Acetamide, N-[5-(4-pyridinyl)-1H-pyrazol-3-yl]- (9CI) (CA INDEX NAME)



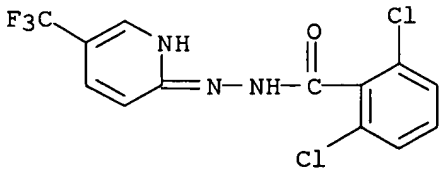
RN 569656-01-5 CAPLUS
CN Benzoic acid, 2-chloro-6-fluoro-, 2-[5-(trifluoromethyl)-2-pyridinyl]hydrazide (9CI) (CA INDEX NAME)



RN 569656-02-6 CAPLUS
CN Benzoic acid, 2,3-dichloro-, 2-[5-(trifluoromethyl)-2-pyridinyl]hydrazide (9CI) (CA INDEX NAME)

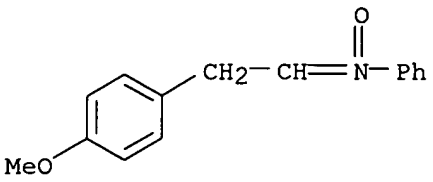


RN 569656-03-7 CAPLUS
CN Benzoic acid, 2,6-dichloro-, 2-[5-(trifluoromethyl)-2-pyridinyl]hydrazide (9CI) (CA INDEX NAME)



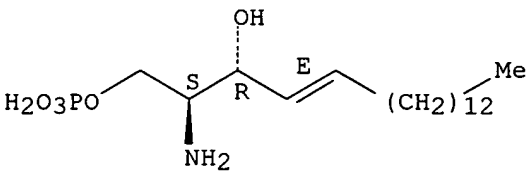
RN 569656-07-1 CAPLUS

CN Benzenamine, N-[2-(4-methoxyphenyl)ethylidene]-, N-oxide (9CI) (CA INDEX NAME)



IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium mobilization stimulated by; Edg receptor modulators for treatment of Edg receptor-associated conditions)
RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



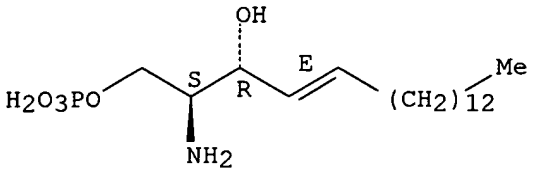
L31 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:703126 CAPLUS
DOCUMENT NUMBER: 141:200234
TITLE: Methods of treating conditions associated with the **Edg-3** receptor
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004167181	A1	20040826	US 2004-760003		20040116
PRIORITY APPLN. INFO.:			US 2003-440322P	P	20030116
			US 2003-454880P	P	20030313

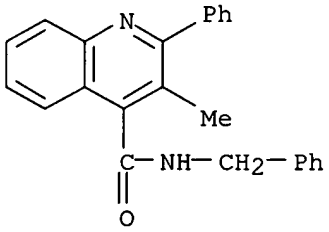
OTHER SOURCE(S): MARPAT 141:200234
AB The invention provides a method of inhibiting the **Edg-3** receptor-mediated biol. activity in a cell. A cell expressing the **Edg-3** receptor is contacted with an amount of an **Edg-3** receptor inhibitor sufficient to inhibit the **Edg-3** receptor-mediated biol. activity. Preferably, the inhibitor is not a phospholipid. Also the invention provides a method where an **Edg-3** receptor-mediated biol. activity is inhibited in a subject. A therapeutically effective amount of an inhibitor of the **Edg-3** receptor is administered to the subject. Preferably, the inhibitor is not a phospholipid.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(methods of treating conditions associated with **Edg-3** receptor)
RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)- (9CI) (CA INDEX NAME)

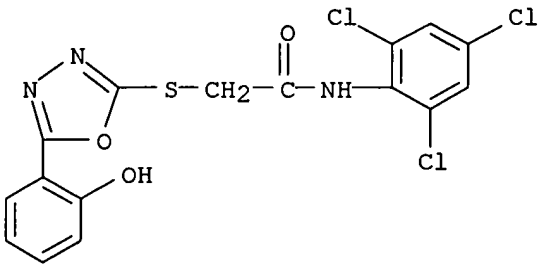
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



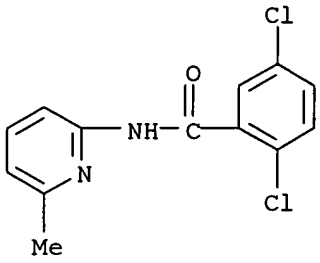
IT **177360-28-0 332161-39-4 346699-98-7 355000-90-7 389079-78-1 569656-28-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating conditions associated with **Edg-3** receptor)
RN 177360-28-0 CAPLUS
CN 4-Quinolinecarboxamide, 3-methyl-2-phenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



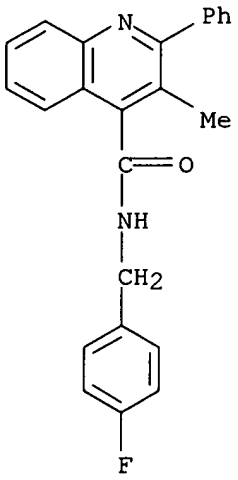
RN 332161-39-4 CAPLUS
CN Acetamide, 2-[[5-(2-hydroxyphenyl)-1,3,4-oxadiazol-2-yl]thio]-N-(2,4,6-trichlorophenyl)- (9CI) (CA INDEX NAME)



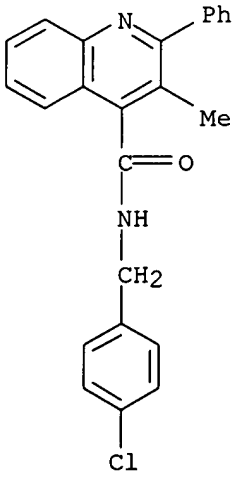
RN 346699-98-7 CAPLUS
CN Benzamide, 2,5-dichloro-N-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)



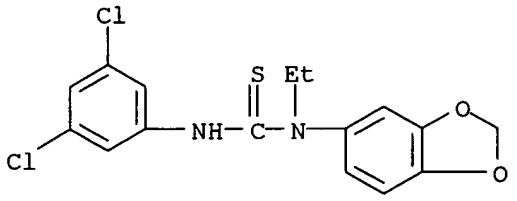
RN 355000-90-7 CAPLUS
CN 4-Quinolinecarboxamide, N-[(4-fluorophenyl)methyl]-3-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 389079-78-1 CAPLUS
CN 4-Quinolinecarboxamide, N-[(4-chlorophenyl)methyl]-3-methyl-2-phenyl- (9CI) (CA INDEX NAME)



RN 569656-28-6 CAPLUS
CN Thiourea, N-1,3-benzodioxol-5-yl-N'-(3,5-dichlorophenyl)-N-ethyl- (9CI) (CA INDEX NAME)



L31 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:703127 CAPLUS
DOCUMENT NUMBER: 141:200235
TITLE: Methods of treating conditions associated with an **Edg-3** receptor
INVENTOR(S): Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

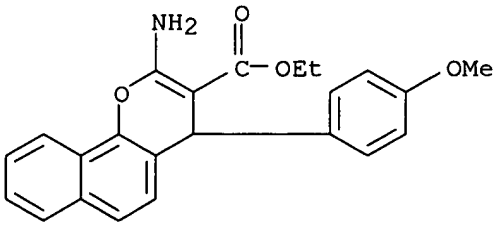
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004167185	A1	20040826	US 2004-760064		20040116
PRIORITY APPLN. INFO.:			US 2003-440325P	P	20030116

OTHER SOURCE(S): MARPAT 141:200235

AB The invention provides a method of inhibiting the **Edg-3** receptor - mediated biol. activity in a cell. A cell expressing the **Edg-3** receptor is contacted with an amount of an **Edg-3** receptor inhibitor sufficient to inhibit the **Edg-3** receptor - mediated biol. activity. Preferably, the inhibitor is not a phospholipid. Also the invention provides a method where an **Edg-3** receptor - mediated biol. activity is inhibited in a subject. A therapeutically effective amount of an inhibitor of the **Edg-3** receptor is administered to the subject. Preferably, the inhibitor is not a phospholipid.

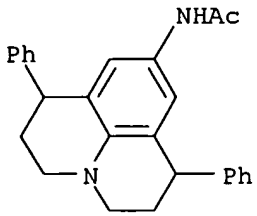
IT **171286-07-0 311773-65-6 329350-38-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of treating conditions associated with **Edg-3** receptor)

RN 171286-07-0 CAPLUS
CN 4H-Naphtho[1,2-b]pyran-3-carboxylic acid, 2-amino-4-(4-methoxyphenyl)-, ethyl ester (9CI) (CA INDEX NAME)

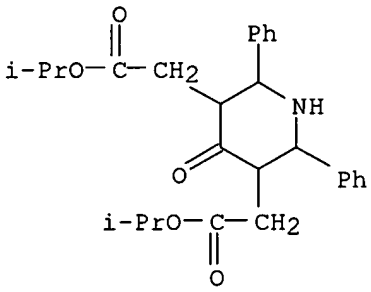


RN 311773-65-6 CAPLUS
CN Acetamide, N-(1,7-diphenyl-2,3,6,7-tetrahydro-1H,5H-benzo[ij]quinolizin-9-

yl)- (9CI) (CA INDEX NAME)



RN 329350-38-1 CAPLUS
CN 3,5-Piperidinediacetic acid, 4-oxo-2,6-diphenyl-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



L31 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:404402 CAPLUS
DOCUMENT NUMBER: 144:425960
TITLE: Estrogen transactivates EGFR via the sphingosine 1-phosphate receptor **Edg-3**: the role of sphingosine kinase-1
AUTHOR(S): Sukocheva, Olga; Wadham, Carol; Holmes, Andrew; Albanese, Nathaniel; Verrier, Emily; Feng, Feng; Bernal, Alex; Derian, Claudia K.; Ullrich, Axel; Vadas, Mathew A.; Xia, Pu
CORPORATE SOURCE: Signal Transduction Laboratory, Division of Human Immunology, Hanson Institute, Institute of Medical and Veterinary Science, Adelaide SA, 5000, Australia
SOURCE: Journal of Cell Biology (2006), 173(2), 301-310
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The transactivation of enhanced growth factor receptor (EGFR) by G protein-coupled receptor (GPCR) ligands is recognized as an important signaling mechanism in the regulation of complex biol. processes, such as **cancer** development. Estrogen (E2), which is a steroid hormone that is intimately implicated in breast **cancer**, has also been suggested to function via EGFR transactivation. In this study, we demonstrate that E2-induced EGFR transactivation in human breast **cancer** cells is driven via a novel signaling system controlled by the lipid kinase sphingosine kinase-1 (SphK1). We show that E2 stimulates SphK1 activation and the release of sphingosine 1-phosphate (S1P), by which E2 is capable of activating the S1P receptor **Edg-3**, resulting in the EGFR transactivation in a matrix metalloprotease-dependent manner. Thus, these findings reveal a key role for SphK1 in the coupling of the signals between three membrane-spanning events induced by

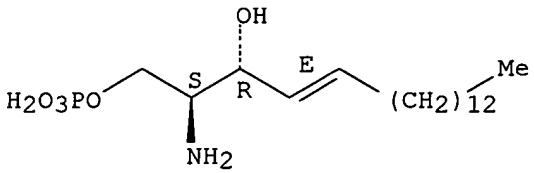
E2, S1P, and EGF. They also suggest a new signal transduction model across three individual ligand-receptor systems, i.e., "criss-cross" transactivation.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(estrogen transactivated EGFR via sphingosine 1-phosphate kinase-1 and its receptor **Edg-3** and ERK pathway)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:615987 CAPLUS
DOCUMENT NUMBER: 143:475738
TITLE: Inhibitory effects of sphingosine 1-phosphate on proliferation of PC-3 human prostate **cancer** cells
AUTHOR(S): Liao, Jia-Jun; Huang, Yu-Ting; Lee, Hsinyu
CORPORATE SOURCE: Department of Life Science, National Taiwan University, Taipei, Taiwan, 106, Peop. Rep. China
SOURCE: Zoological Studies (2005), 44(2), 219-227
CODEN: ZOSTEG; ISSN: 1021-5506
PUBLISHER: Academia Sinica, Institute of Zoology
DOCUMENT TYPE: Journal
LANGUAGE: English

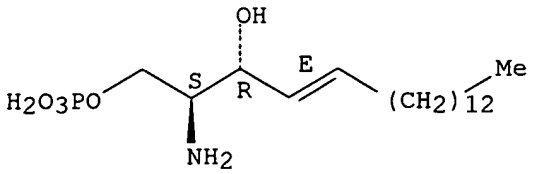
AB Prostate **cancer** is the most-common **cancer** in adult men and the 2nd-leading cause of **cancer** deaths in Western countries. Although androgens and peptide growth factors have been implicated in this disease, determinants of the pathol. growth of prostate **cancer** are still unclear. Lysophosphatidic acid (LPA) and sphingosine 1-phosphate (S1P) are both potent lysophospholipid growth factors with diverse biol. activities and have been suggested as being important in regulating the proliferation and metastasis of **cancer** cells. LPA activates the ERK pathway and induces proliferation of the human prostate **cancer** cell line, PC-3. However, the effect of S1P on prostate **cancer** is still poorly understood. In this study, we found that S1P inhibited cell proliferation through an apoptosis-independent and necrosis-dependent mechanism and caused cell cycle arrest in the G1 phase of PC-3 cells. S1P also induced significant rounding of cells and actin reorganization. These effects are likely mediated through activation of the S1P5 receptor. In conclusion, we propose that S1P might change cell-ECM interactions through cytoskeletal rearrangement, thereby influencing the proliferation of prostate **cancer** cells.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of inhibitory effects of sphingosine 1-phosphate on proliferation of PC-3 human prostate **cancer** cells)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-
(9CI) (CA INDEX NAME)

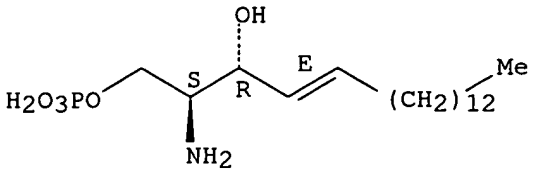
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:124915 CAPLUS
DOCUMENT NUMBER: 138:367328
TITLE: Modulation of sphingosine 1-phosphate/EDG signaling by **tumor** necrosis factor-α in vascular endothelial cells
AUTHOR(S): Osada, Makoto; Yatomi, Yutaka; Ohmori, Tsukasa; Hosogaya, Shigemi; Ozaki, Yukio
CORPORATE SOURCE: Department of Clinical Laboratory, Yamanashi Medical University Hospital, Yamanashi, Nakakoma, 409-3898, Japan
SOURCE: Thrombosis Research (2003), Volume Date 2002, 108(2-3), 169-174
CODEN: THBRAA; ISSN: 0049-3848
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sphingosine 1-phosphate (Sph-1-P) is a lysophospholipid mediator which is present in plasma and other body fluids and exerts potent and pleiotropic biol. effects. Such extracellular mediator activities of Sph-1-P are mainly regulated by subfamilies of G protein-coupled receptors, of which the most completely characterized are those encoded by the endothelial differentiation genes (EDGs). A study was conducted to determine the effects of **tumor** necrosis factor-α (TNF-α) on the expression of the Sph-1-P receptors EDG-1 and **EDG-3** and on Sph-1-P-induced intracellular Ca2+ mobilization in human umbilical vein endothelial cells (HUVECs). **EDG-3** was downregulated by TNF-α, while the EDG-1 expression was not affected in HUVECs. Sph-1-P-induced Ca2+ mobilization and cytoskeletal reorganization and the resultant migration were modulated by TNF-α. The finding that HUVECs responses to Sph-1-P may be modulated by TNF-α (possibly via regulation of **EDG-3** expression) seems important when it is interpreted as a point of contact between inflammation and thrombosis and homeostasis.
IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine 1-phosphate/EDG signaling modulation by **tumor** necrosis factor-α in vascular endothelium in relation to inflammation vs. thrombosis/hemostasis)
RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

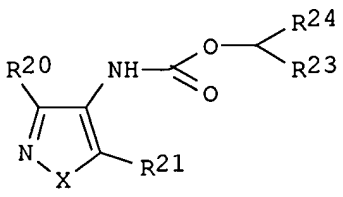


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409218 CAPLUS
DOCUMENT NUMBER: 142:441857
TITLE: Methods of treating conditions associated with an edg-2 receptor
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Spencer, Juliet; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 347,420, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005101518	A1	20050512	US 2003-390427		20030314
PRIORITY APPLN. INFO.:			US 2002-350448P	P	20020118
			US 2003-347420	B2	20030117

OTHER SOURCE(S): MARPAT 142:441857
GI



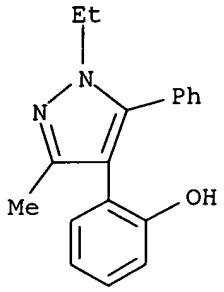
I

AB In one aspect, the present invention provides a method for modulating an Edg-2 receptor mediated biol. activity in a cell. A cell expressing the Edg-2 receptor is contacted with an modulator with formula I (where X = O, S; R20 = alkyl aryl, etc., R21 = alkyl, substituted alkyl, etc., R23 = H, alkyl, substituted alkyl; R24 = aryl, etc.) of the Edg-2 receptor, which modulates the Edg-2 receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating Edg-2 receptor mediated biol. activity in a subject. A therapeutically effective amount of an modulator of the Edg-2 receptor is administered to the subject.

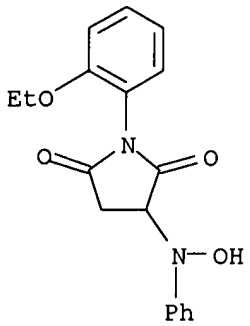
IT **173275-26-8P 353273-74-2P 569656-26-4P 569656-27-5P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of treating conditions associated with an edg-2 receptor)

RN 173275-26-8 CAPLUS
CN Phenol, 2-(1-ethyl-3-methyl-5-phenyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX

NAME)

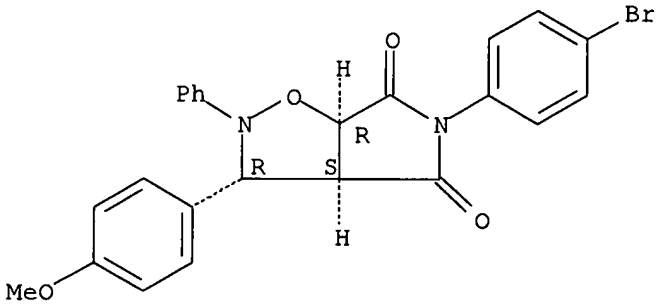


RN 353273-74-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)- (9CI) (CA INDEX NAME)



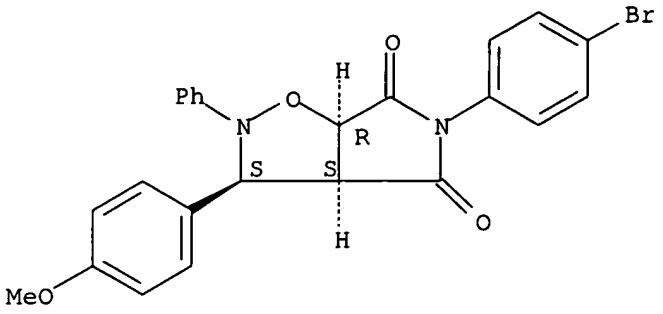
RN 569656-26-4 CAPLUS
CN 2H-Pyrrolo[3,4-d]isoxazole-4,6(3H,5H)-dione, 5-(4-bromophenyl)dihydro-3-(4-methoxyphenyl)-2-phenyl-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

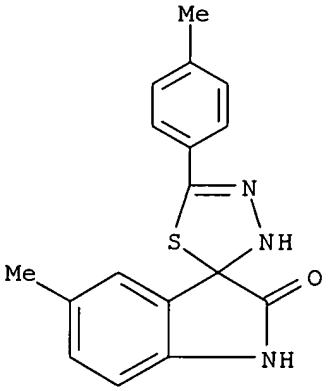


RN 569656-27-5 CAPLUS
CN 2H-Pyrrolo[3,4-d]isoxazole-4,6(3H,5H)-dione, 5-(4-bromophenyl)dihydro-3-(4-methoxyphenyl)-2-phenyl-, (3S,3aS,6aR)- (9CI) (CA INDEX NAME)

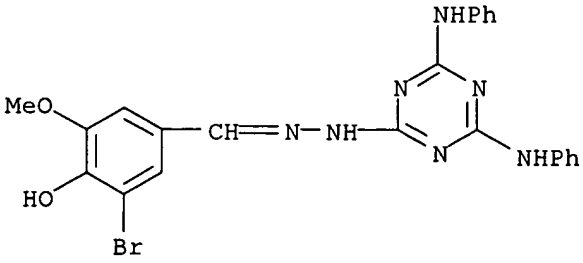
Absolute stereochemistry.



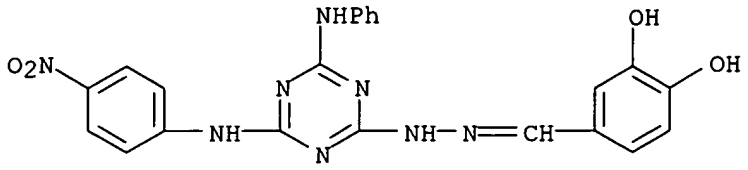
IT **309282-30-2P 322662-05-5P 330630-42-7P 353793-15-4P 383164-60-1P 569656-23-1P 569656-24-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of treating conditions associated with an edg-2 receptor)
RN 309282-30-2 CAPLUS
CN Spiro[3H-indole-3,2'(3'H)-[1,3,4]thiadiazol]-2(1H)-one, 5-methyl-5'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



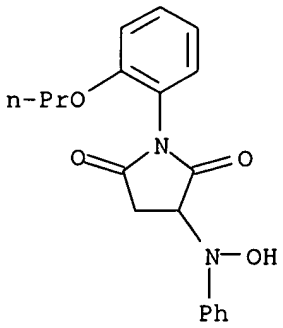
RN 322662-05-5 CAPLUS
CN Benzaldehyde, 3-bromo-4-hydroxy-5-methoxy-, [4,6-bis(phenylamino)-1,3,5-triazin-2-yl]hydrazone (9CI) (CA INDEX NAME)



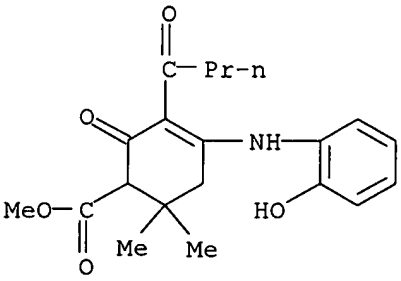
RN 330630-42-7 CAPLUS
CN Benzaldehyde, 3,4-dihydroxy-, [4-[(4-nitrophenyl)amino]-6-(phenylamino)-1,3,5-triazin-2-yl]hydrazone (9CI) (CA INDEX NAME)



RN 353793-15-4 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(hydroxyphenylamino)-1-(2-propoxyphenyl)- (9CI) (CA INDEX NAME)

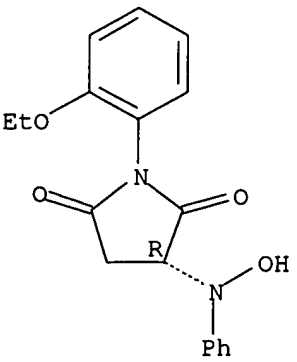


RN 383164-60-1 CAPLUS
CN 3-Cyclohexene-1-carboxylic acid, 4-[(2-hydroxyphenyl)amino]-6,6-dimethyl-2-oxo-3-(1-oxobutyl)-, methyl ester (9CI) (CA INDEX NAME)



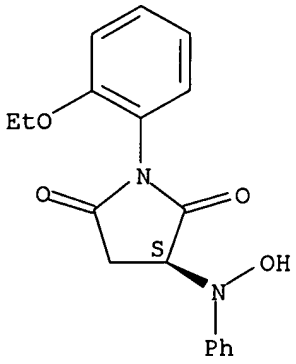
RN 569656-23-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 569656-24-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)-, (3S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:80878 CAPLUS
DOCUMENT NUMBER: 140:139547
TITLE: Screening for substituted aryl isoxazole effectors of the Edg-1 receptor for the treatment of receptor-associated conditions
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Gluchowski, Charles; Spencer, Juliet V.
PATENT ASSIGNEE(S): Ceretek Llc, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004009816	A1	20040129	WO 2003-US22463		20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2466288	AA	20040129	CA 2003-2466288		20030717
AU 2003252023	A1	20040209	AU 2003-252023		20030717
US 2004147562	A1	20040729	US 2003-621966		20030717
EP 1523556	A1	20050420	EP 2003-765716		20030717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005533852	T2	20051110	JP 2004-523557		20030717
PRIORITY APPLN. INFO.:			US 2002-397299P	P	20020718
			WO 2003-US22463	W	20030717

OTHER SOURCE(S): MARPAT 140:139547
AB In one aspect, the present invention provides a method of modulating an Edg-1 receptor mediated biol. activity in a cell. A cell expressing the

Edg-1 receptor is contacted with a modulator of the Edg-1 receptor sufficient to modulate the Edg-1 receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-1 receptor mediated biol. activity in a subject. A therapeutically effective amount of a modulator of the Edg-1 receptor is administered to the subject.

IT **182762-25-0**, GenBank X83864 **218763-60-1**, GenBank AJ000479 **259476-69-2**, GenBank AF233092 **384729-36-6**, GenBank U78192 **385223-15-4**, GenBank AF011466 **390105-18-7**, GenBank AF034780 **390174-36-4**, GenBank AF233365 **390523-03-2**, GenBank AF317676 **392101-34-7**, GenBank AF127138
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(screening for substituted aryl isoxazole effectors of Edg-1 receptor for treatment of receptor-associated conditions)

RN 182762-25-0 CAPLUS
CN DNA (human gene EDG-3 plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 218763-60-1 CAPLUS
CN DNA (human dendritic cell gene EDG6 G protein-coupled receptor cDNA plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 259476-69-2 CAPLUS
CN DNA (human gene EDG4 lysophosphatidic acid receptor 4 cDNA plus flanks) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 384729-36-6 CAPLUS
CN GenBank U78192 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 385223-15-4 CAPLUS
CN GenBank AF011466 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 390105-18-7 CAPLUS
CN GenBank AF034780 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 390174-36-4 CAPLUS
CN DNA (human gene CHEDG1 cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 390523-03-2 CAPLUS
CN GenBank AF317676 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 392101-34-7 CAPLUS
CN GenBank AF127138 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259685 CAPLUS
DOCUMENT NUMBER: 142:309943
TITLE: Methods using Edg-2 receptor modulators for treatment of edg-2 receptor-associated conditions
INVENTOR(S): Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet

V.; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

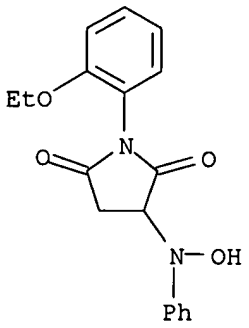
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005065194	A1	20050324	US 2004-760061		20040116
PRIORITY APPLN. INFO.:			US 2003-440341P	P	20030116

OTHER SOURCE(S): MARPAT 142:309943

AB In one aspect, the invention provides a method for modulating an Edg-2 receptor-mediated biol. activity in a cell. A cell expressing the Edg-2 receptor is contacted with an modulator of the Edg-2 receptor, which modulates the Edg-2 receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating Edg-2 receptor mediated biol. activity in a subject. A therapeutically effective amount of an modulator of the Edg-2 receptor is administered to the subject. Compds. of the invention include pyrrolidine-2,5-dione derivs. (preparation included).

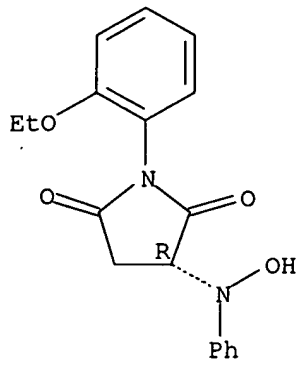
IT **353273-74-2P 569656-23-1P 569656-24-2P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg-2 receptor modulators for treatment of edg-2 receptor-associated conditions)

RN 353273-74-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)- (9CI) (CA INDEX NAME)



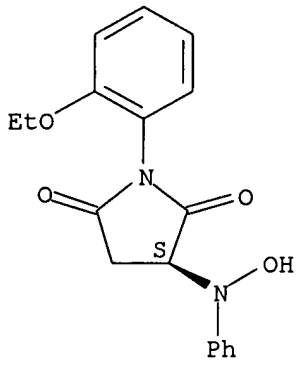
RN 569656-23-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

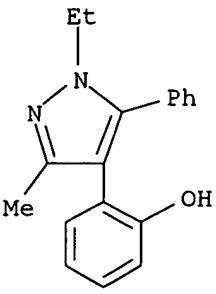


RN 569656-24-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-(hydroxyphenylamino)-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

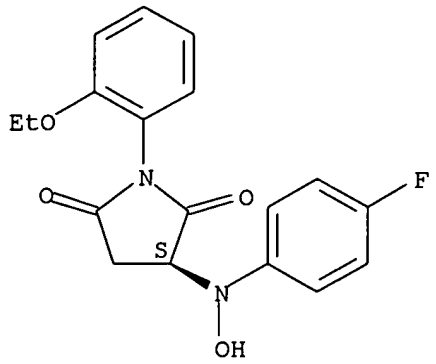


IT **173275-26-8P 569656-25-3P 569656-26-4P 569656-27-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg-2 receptor modulators for treatment of edg-2 receptor-associated conditions)
RN 173275-26-8 CAPLUS
CN Phenol, 2-(1-ethyl-3-methyl-5-phenyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)



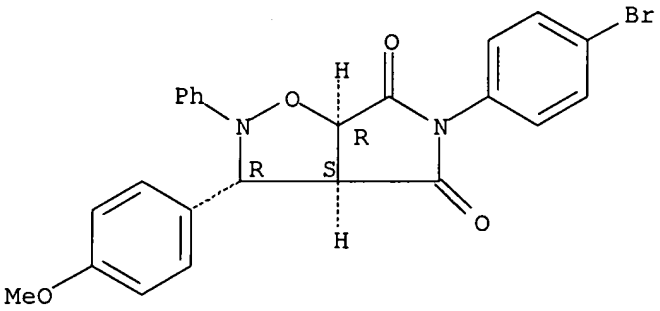
RN 569656-25-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-(2-ethoxyphenyl)-3-[(4-fluorophenyl)hydroxyamino]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



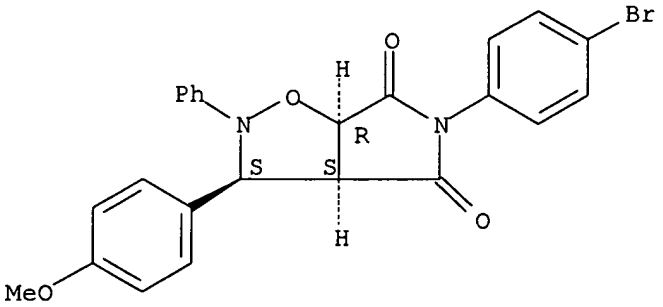
RN 569656-26-4 CAPLUS
CN 2H-Pyrrolo[3,4-d]isoxazole-4,6(3H,5H)-dione, 5-(4-bromophenyl)dihydro-3-(4-methoxyphenyl)-2-phenyl-, (3R,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



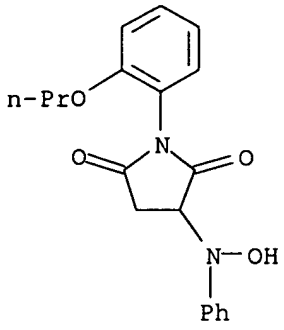
RN 569656-27-5 CAPLUS
CN 2H-Pyrrolo[3,4-d]isoxazole-4,6(3H,5H)-dione, 5-(4-bromophenyl)dihydro-3-(4-methoxyphenyl)-2-phenyl-, (3S,3aS,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **353793-15-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Edg-2 receptor modulators for treatment of edg-2 receptor-associated conditions)
RN 353793-15-4 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(hydroxyphenylamino)-1-(2-propoxyphenyl)- (9CI)

(CA INDEX NAME)



L31 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1242755 CAPLUS
DOCUMENT NUMBER: 143:472565
TITLE: Methods of treating conditions associated with an Edg-7 receptor
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S. Ser. No. 352,579.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005261298	A1	20051124	US 2003-390428	20030314
WO 2003062392	A2	20030731	WO 2003-US1881	20030121
WO 2003062392	A3	20050120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

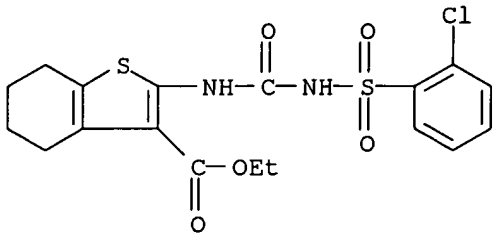
US 2002-350446P	P	20020118
WO 2003-US1881	A1	20030121
US 2003-352579	B2	20030127
US 2002-350445P	P	20020118
US 2002-350447P	P	20020118
US 2002-350448P	P	20020118

OTHER SOURCE(S): MARPAT 143:472565

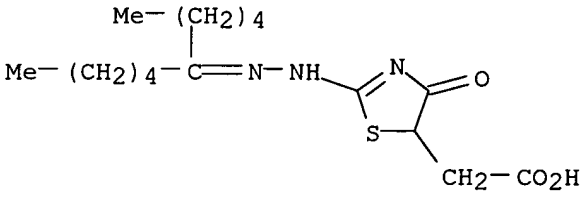
AB In one aspect, the present invention provides a method for modulating an Edg-7 receptor mediated biol. activity in a cell. A cell expressing the Edg-7 receptor is contacted with a modulator of the Edg-7 receptor which is capable of modulating an Edg-7 receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-7 receptor mediated biol. activity in a subject. A therapeutically effective amount of a modulator of the Edg-7 receptor is administered to the subject.

IT **306764-68-1P 312501-62-5P 331945-22-3P 353771-45-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Edg-7 modulators for treating conditions associated with Edg-7 receptor)

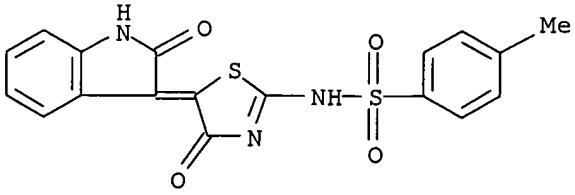
RN 306764-68-1 CAPLUS
CN Benzo[b]thiophene-3-carboxylic acid, 2-[[[[(2-chlorophenyl)sulfonyl]amino]carbonyl]amino]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)



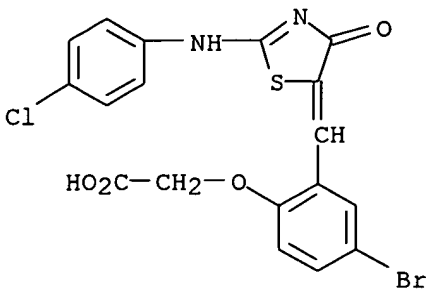
RN 312501-62-5 CAPLUS
CN 5-Thiazoleacetic acid, 4,5-dihydro-4-oxo-2-[(1-pentylhexylidene)hydrazino]- (9CI) (CA INDEX NAME)



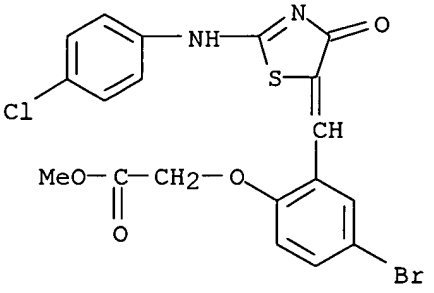
RN 331945-22-3 CAPLUS
CN Benzenesulfonamide, N-[5-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)-4,5-dihydro-4-oxo-2-thiazolyl]-4-methyl- (9CI) (CA INDEX NAME)



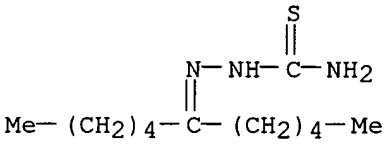
RN 353771-45-6 CAPLUS
CN Acetic acid, [4-bromo-2-[[2-[(4-chlorophenyl)amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenoxy]- (9CI) (CA INDEX NAME)



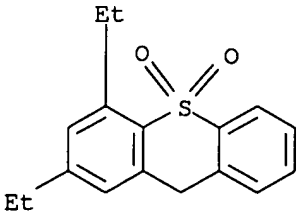
IT **569656-05-9 569656-06-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Edg-7 modulators for treating conditions associated with Edg-7 receptor)
RN 569656-05-9 CAPLUS
CN Acetic acid, [4-bromo-2-[[2-[(4-chlorophenyl)amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 569656-06-0 CAPLUS
CN Hydrazinecarbothioamide, 2-(1-pentylhexylidene)- (9CI) (CA INDEX NAME)



IT **569656-29-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Edg-7 modulators for treating conditions associated with Edg-7 receptor)
RN 569656-29-7 CAPLUS
CN 9H-Thioxanthene, 2,4-diethyl-, 10,10-dioxide (9CI) (CA INDEX NAME)



L31 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

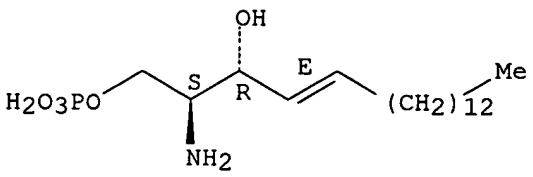
ACCESSION NUMBER: 2000:41832 CAPLUS
DOCUMENT NUMBER: 132:189393
TITLE: Sphingosine-1-phosphate inhibits motility of human breast **cancer** cells independently of cell surface receptors
AUTHOR(S): Wang, Fang; Van Brocklyn, James R.; Edsall, Lisa; Nava, Victor E.; Spiegel, Sarah
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC, 20007, USA
SOURCE: Cancer Research (1999), 59(24), 6185-6191
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Exogenous sphingosine-1-phosphate (SPP) inhibits chemotactic motility of several transformed cell lines. We have found that SPP at high micromolar concns. decreased chemotaxis of estrogen-independent (MDA-MB-231 and BT 549) and estrogen-dependent (MCF-7 and ZR-75-1) human breast **cancer** cells. Because SPP has been implicated as a lipid-signaling mol. with novel dual intra- and intercellular actions, it was of interest to determine whether the effect of SPP on chemotactic motility of human breast **cancer** cells is mediated intracellularly or through the recently identified endothelial differentiation gene (EDG) family of G protein-coupled SPP receptors. There was no detectable specific binding of [32P]SPP to MDA-MB-231 or MCF-7 cells; however, reverse transcription-PCR anal. revealed that both MDA-MB-231 and MCF-7 cells expressed moderate levels of **EDG-3**, neither expressed EDG-1, and EDG-5 mRNA was expressed in MCF-7 but not in MDA-MB-231 cells. In contrast to SPP, sphinganine-1-phosphate, which binds to and signals through SPP receptors EDG-1, **EDG-3**, and EDG-5, had no effect on chemotactic motility of MDA-MB-231 or MCF-7 cells. To further discriminate between intracellular and receptor-mediated actions of SPP, we used caged SPP, a photolyzable derivative of SPP that elevates intracellular levels of SPP after illumination. Caged SPP inhibited chemotactic motility of MDA-MB-231 cells only upon UV irradiation In addition, in MCF-7 cells, overexpression of sphingosine kinase, the enzyme that produces SPP, inhibited chemotactic motility compared with vector-transfected cells and markedly increased cellular SPP levels in the absence of detectable secretion. Our results suggest that the inhibitory effect of SPP on chemotactic motility of human breast **cancer** cells is likely mediated through intracellular actions of SPP rather than through cell surface receptors.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(sphingosine-1-phosphate inhibits motility of human breast **cancer** cells independently of cell surface receptors)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

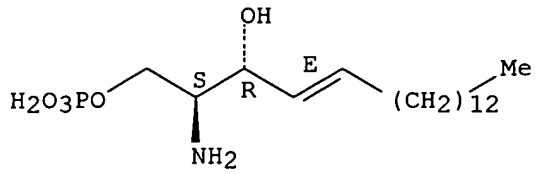
L31 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:21946 CAPLUS
DOCUMENT NUMBER: 144:485755
TITLE: Sphingosine 1-phosphate receptor expression profile in human gastric **cancer** cells: differential regulation on the migration and proliferation
AUTHOR(S): Yamashita, Hiroharu; Kitayama, Joji; Shida, Dai; Yamaguchi, Hironori; Mori, Ken; Osada, Makoto; Aoki, Shinya; Yatomi, Yutaka; Takuwa, Yoh; Nagawa, Hirokazu
CORPORATE SOURCE: Department of Surgical Oncology, University of Tokyo Graduate School of Medicine, Tokyo, Japan
SOURCE: Journal of Surgical Research (2006), 130(1), 80-87
CODEN: JSGRA2; ISSN: 0022-4804
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sphingosine 1-phosphate (S1P) is a bioactive lysophospholipid, derived from activated platelet, that is known to induce diverse cellular responses through at least five G-protein-coupled receptors on various cell types. Abnormal platelet and coagulation activation is often seen in patients with gastric **cancer**. However, neither the effects of this platelet-derived mediator S1P nor the distribution of S1P receptors on the gastric **cancer** cell are fully understood. The aim of this study was to examine the possible role of S1P and its receptors in the progression of gastric **cancer**. We characterized the expression profiles of S1P receptors in nine human gastric **cancer** cell lines and evaluated the relationship between the responses to S1P and its receptor expression on cell migration by modified Boyden chamber and cell proliferation by MTS assay. Northern blotting anal. has revealed that S1P2 was expressed in all gastric **cancer** cell lines to varying degrees, and S1P3 was expressed in four cell lines. S1P1 expression was weak, and no significant expression of either S1P4 or S1P5 was detected. The addition of S1P markedly stimulated the migration of MKN1 and HCG-27 that dominantly expressed S1P3, and the effect was potently inhibited by pertussis toxin or wortmannin. In contrast, SIP significantly inhibited the migration of AZ-521 that expressed S1P2 exclusively. This indicates that the balance between S1P2- and S1P3-mediated signals might be critical in determining the metastatic response of gastric **cancer** cells to S1P. S1P elicited weak but significant antiproliferative effects on all of the three cell lines, although the effects were not major. In these cells, S1P induced extracellular signal-regulated kinase (ERK) phosphorylation with transient Akt dephosphorylation that may cause the weak effects on proliferation. Our results suggest that the S1P receptor expression may critically determine the biol. behavior of gastric **cancers** and thus therapeutic interventions directed at each S1P receptor might be clin. effective in preventing metastasis in gastric **cancer**.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine 1-phosphate 1 expressed in MKN45 gastric **cancer** cell line)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:703129 CAPLUS
DOCUMENT NUMBER: 141:218996
TITLE: Methods using Edg-7 modulators for treating conditions associated with an Edg-7 receptor
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004167192	A1	20040826	US 2004-760002		20040116
PRIORITY APPLN. INFO.:			US 2003-440321P	P	20030116
			US 2003-454881P	P	20030313

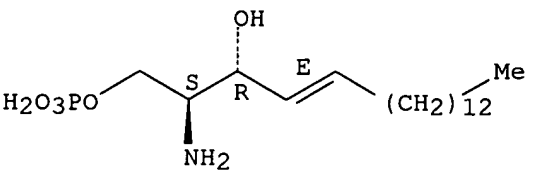
OTHER SOURCE(S): MARPAT 141:218996

AB The invention provides a method for modulating an Edg-7 receptor mediated biol. activity in a cell. A cell expressing the Edg-7 receptor is contacted with a modulator of the Edg-7 receptor which is capable of modulating an Edg-7 receptor-mediated biol. activity. The invention also provides a method for modulating an Edg-7 receptor-mediated biol. activity in a subject. A therapeutically effective amount of a modulator of the Edg-7 receptor is administered to the subject. Preparation of e.g. 4-Bromo-2-[2-(4-chlorophenylamino)-4-oxothiazolidin-5-ylidenemethyl]phenoxyacetic acid is described.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Edg-7 modulators for treating conditions associated with an Edg-7 receptor)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

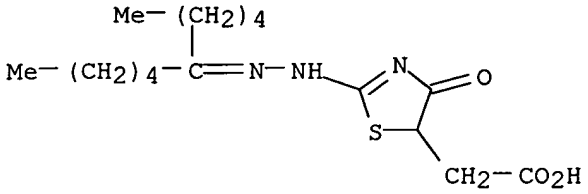


IT **312501-62-5P 331945-22-3P 353771-45-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(Edg-7 modulators for treating conditions associated with an Edg-7 receptor)

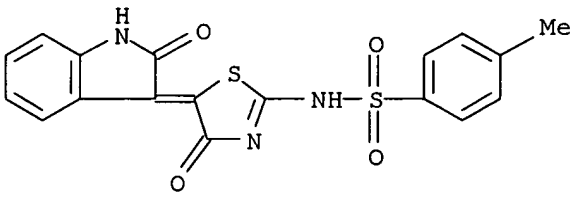
RN 312501-62-5 CAPLUS

CN 5-Thiazoleacetic acid, 4,5-dihydro-4-oxo-2-[(1-pentylhexylidene)hydrazino]- (9CI) (CA INDEX NAME)



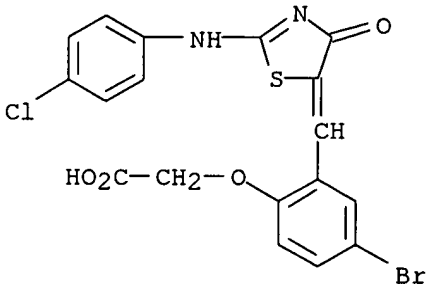
RN 331945-22-3 CAPLUS

CN Benzenesulfonamide, N-[5-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)-4,5-dihydro-4-oxo-2-thiazolyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 353771-45-6 CAPLUS

CN Acetic acid, [4-bromo-2-[[2-[(4-chlorophenyl)amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenoxy]- (9CI) (CA INDEX NAME)

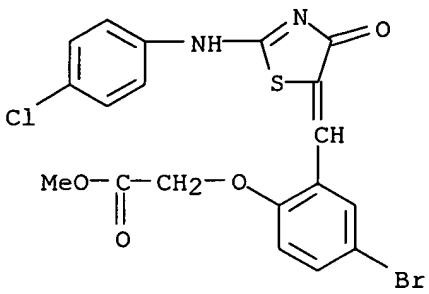


IT **569656-05-9 569656-06-0**

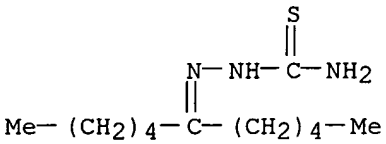
RL: RCT (Reactant); RACT (Reactant or reagent)
(Edg-7 modulators for treating conditions associated with an Edg-7 receptor)

RN 569656-05-9 CAPLUS

CN Acetic acid, [4-bromo-2-[[2-[(4-chlorophenyl)amino]-4-oxo-5(4H)-thiazolylidene]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 569656-06-0 CAPLUS
CN Hydrazinecarbothioamide, 2-(1-pentylhexylidene)- (9CI) (CA INDEX NAME)



L31 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:693647 CAPLUS
DOCUMENT NUMBER: 132:21672
TITLE: Distinctive expression and functions of the type 4 endothelial differentiation gene-encoded G protein-coupled receptor for lysophosphatidic acid in ovarian **cancer**
AUTHOR(S): Goetzl, Edward J.; Dolezalova, Hana; Kong, Yvonne; Hu, Yu-Long; Jaffe, Robert B.; Kalli, Kimberly R.; Conover, Cheryl A.
CORPORATE SOURCE: Departments of Medicine and Microbiology-Immunology, University of California, San Francisco, CA, 94143, USA
SOURCE: Cancer Research (1999), 59(20), 5370-5375
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Endothelial differentiation gene (edg)-encoded G protein-coupled receptors (Edg Rs)-1, -3, and -5 bind sphingosine 1-phosphate (S1P), and Edg-2 and -4 bind lysophosphatidic acid (LPA). Edg Rs transduce signals from LPA and S1P that stimulate ras- and rho-dependent cellular proliferation, enhance cellular survival, and suppress apoptosis. That high levels of LPA in plasma and ascitic fluid of patients with ovarian **cancer** correlate with widespread invasion suggested the importance of investigating expression and functions of Edg Rs in ovarian **cancer** cells (OCCs) as compared with nonmalignant ovarian surface epithelial cells (OSEs). Analyses of Edg Rs by semiquant. reverse transcription-PCR, a radioactively quantified variant of PCR, and Western blots developed with monoclonal antibodies showed prominent expression of Edg-4 R in primary cultures and established lines of OCCs but none in OSEs. In contrast, levels of Edg-2, -3, and -5 were higher in OSEs than OCCs. LPA stimulated proliferation and signaled a serum response element-luciferase reporter of immediate-early gene activation in OCCs but not OSEs, whereas S1P evoked similar responses in both OSEs and OCCs. Pharmacol. inhibitors of Edg R signaling suppressed OCC responses to LPA. A combination of monoclonal anti-Edg-4 R antibody and phorbol myristate acetate, which were inactive sep., evoked proliferative and serum response element-luciferase responses of OCCs but not OSEs. Thus the Edg-4 R may represent a

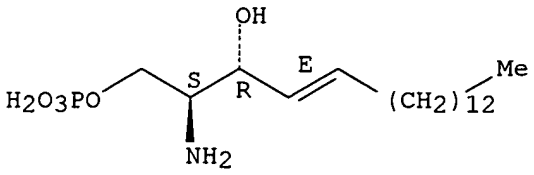
distinctive marker of OCC that transduces growth-promoting signals from the high local concns. of LPA characteristic of aggressive ovarian **cancer**.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(signaling; distinctive expression and functions of type 4 endothelial differentiation gene-encoded G protein-coupled receptor for lysophosphatidic acid in human ovarian **cancer** in relation to)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:733793 CAPLUS
DOCUMENT NUMBER: 139:336148
TITLE: Autotaxin hydrolyzes sphingosylphosphorylcholine to produce the regulator of migration, sphingosine-1-phosphate
AUTHOR(S): Clair, Timothy; Aoki, Junken; Koh, Eunjin; Bandle, Russell W.; Nam, Suk Woo; Ptaszynska, Malgorzata M.; Mills, Gordon B.; Schiffmann, Elliott; Liotta, Lance A.; Stracke, Mary L.
CORPORATE SOURCE: Laboratory of Pathology, National Cancer Institute, NIH, Bethesda, MD, 20892, USA
SOURCE: Cancer Research (2003), 63(17), 5446-5453
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Autotaxin (ATX) is an exoenzyme that potently induces **tumor** cell motility, and enhances exptl. metastasis and angiogenesis. ATX was shown recently to be identical to serum lysophospholipase D activity, producing lysophosphatidic acid (LPA) from lysoglycerophospholipids. LPA, itself a strong chemoattractant for **tumor** cells, may mediate the actions of ATX. The authors now extend the substrate specificity to sphingosylphosphorylcholine (SPC), which ATX hydrolyzes to sphingosine-1-phosphate (S1P). Under migration assay conditions, this novel reaction for the production of S1P has a substrate (SPC) Km = 0.23 mM. In the authors' responder cell lines (NIH3T3 clone7 and A2058), S1P exerts maximal biol. effects at concns. of 10-100 nM and is mimicked in its biol. effects by ATX plus SPC. These effects include inhibition of ATX- and LPA-stimulated motility, and elevation of activated Rho. In NIH3T3 clone7 cells stimulated with platelet-derived growth factor and treated with 10-25 nM S1P, motility is not inhibited and activation of Rho is unaffected, indicating that S1P possesses specificity in its effects. The exoenzyme ATX can potentially regulate diverse processes such as motility and angiogenesis via the S1P family of receptors. Because ATX hydrolyzes nucleotides, lysoglycerophospholipids, and phosphosphingolipids into

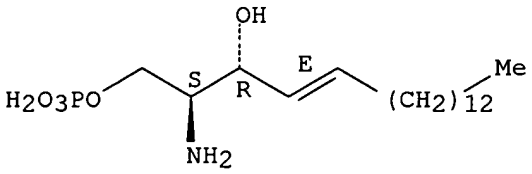
bioactive products, it possesses the ability, depending on the availability of substrates, to act as pos. or neg. regulator of receptor-mediated activity in the cellular microenvironment.

IT **26993-30-6**, Sphingosine-1-Phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autotaxin hydrolyzes sphingosylphosphorylcholine to produce regulator of migration, sphingosine-1-phosphate, in relation to **tumor** cell migration)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:606760 CAPLUS
DOCUMENT NUMBER: 131:320907
TITLE: Dual mechanisms for lysophospholipid induction of proliferation of human breast carcinoma cells
AUTHOR(S): Goetzl, Edward J.; Dolezalova, Hana; Kong, Yvonne; Zeng, Li
CORPORATE SOURCE: Departments of Medicine and Microbiology-Immunology, University of California Medical Center, San Francisco, CA, 94143-0711, USA
SOURCE: Cancer Research (1999), 59(18), 4732-4737
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Endothelial differentiation gene-encoded G protein-coupled receptors (Edg Rs) Edg-1, **Edg-3**, and Edg-5 bind sphingosine 1-phosphate (S1P), and Edg-2 and Edg-4 Rs bind lysophosphatidic acid (LPA). LPA and S1P initiate ras- and rho-dependent signaling of cellular growth. Cultured lines of human breast **cancer** cells (BCCs) express **Edg-3** > Edg-4 > Edg-5 > or = Edg-2, without detectable Edg-1, by both assessment of mRNA and Western blots with rabbit and monoclonal mouse anti-Edg R antibodies. BCC proliferation was stimulated significantly by 10-9 M to 10-6 M LPA and S1P. Luciferase constructs containing the serum response element (SRE) of growth-related gene promoters reported mean activation of BCCs by LPA and S1P of up to 85-fold. LPA and S1P stimulated BCC secretion of type II insulin-like growth factor (IGF-II) by 2-7-fold, to levels at which exogenous IGF-II stimulated increased proliferation and SRE activation of BCCs. All BCC responses to LPA and S1P were suppressed similarly by pertussis toxin, mitogen-activated protein kinase kinase inhibitors, and C3 exoenzyme inactivation of rho, suggesting mediation by Edg Rs. Monoclonal anti-IGF-II and anti-IGFR1 antibodies suppressed proliferation and SRE reports of BCCs to LPA and S1P by means of up to 65%. Edg Rs thus transduce LPA and S1P enhancement of BCC growth, both directly through SRE and indirectly by enhancing the contribution of IGF-II.

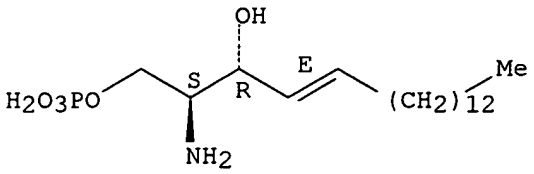
IT **26993-30-6**, Sphingosine 1-phosphate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(induction of proliferation of human breast carcinoma cells)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:703124 CAPLUS

DOCUMENT NUMBER: 141:218944

TITLE: Treating conditions associated with an Edg-7 receptor

INVENTOR(S): Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet V.; Gluchowski, Charles

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 29 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

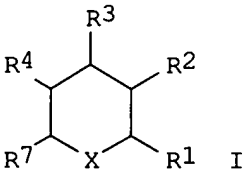
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

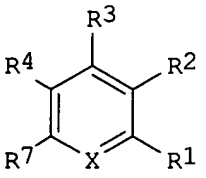
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004167165	A1	20040826	US 2004-760062		20040116
PRIORITY APPLN. INFO.:			US 2003-440336P	P	20030116

OTHER SOURCE(S): MARPAT 141:218944

GI



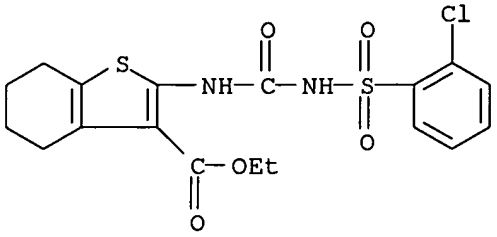
I



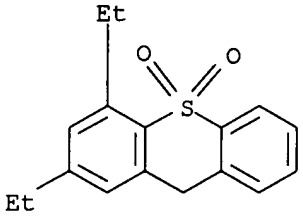
II

AB The invention provides a method for modulating an Edg-7 receptor mediated biol. activity in a cell. A cell expressing the Edg-7 receptor is contacted with a modulator of the Edg-7 receptor which is capable of modulating an Edg-7 receptor mediated biol. activity. The invention provides a method for modulating an Edg-7 receptor mediated biol. activity in a subject. A therapeutically effective amount of the Edg-7 receptor modulator with formula I (where R1,R2 R3 R4 and R7 = -H,-halo,-CN, -NO2 etc. independently) or with formula II (where R1, R2, R3, R4 and R7 = -H,-halo, -NO2 -CN, etc.) or a pharmaceutically available solvate or hydrate therof is administered to the subject.

IT **306764-68-1P 569656-29-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods of treating conditions associated with an Edg-7 receptor)
RN 306764-68-1 CAPLUS
CN Benzo[b]thiophene-3-carboxylic acid, 2-[[[[(2-chlorophenyl)sulfonyl]amino]carbonyl]amino]-4,5,6,7-tetrahydro-, ethyl ester (9CI) (CA INDEX NAME)



RN 569656-29-7 CAPLUS
CN 9H-Thioxanthene, 2,4-diethyl-, 10,10-dioxide (9CI) (CA INDEX NAME)



L31 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:125122 CAPLUS
DOCUMENT NUMBER: 139:33670
TITLE: Effects of sphingosine-1-phosphate and lysophosphatidic acid on human osteoblastic cells
AUTHOR(S): Dziak, R.; Yang, B. M.; Leung, B. W.; Li, S.; Marzec, N.; Margarone, J.; Bobek, L.
CORPORATE SOURCE: Departments of Oral Biology and Endodontics, School of Dental Medicine, The State University of New York, The University at Buffalo, Buffalo, NY, 14214, USA
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (2003), 68(3), 239-249
CODEN: PLEAEU; ISSN: 0952-3278
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of the lysophospholipids, sphingosine-1-phosphate (S1P) and lysophosphatidic acid (LPA) were studied in human primary osteoblastic cells and the human osteosarcomal cell lines, G292 and MG-63. The studies focused on the role of the Gi protein in the regulation of S1P and LPA-induced proliferation, the effects of the phospholipids on alkaline phosphatase, an early marker of osteoblastic cell proliferation, and the presence of edg receptors. Proliferation was assessed by 3H-thymidine incorporation. Short-term incubation with S1P or LPA induced increases in proliferation that were attenuated in the presence of the Gi inhibitor, pertussis toxin. Alkaline phosphatase activity was measured with a spectrophotometric assay. Biphasic effects of S1P and LPA were observed with

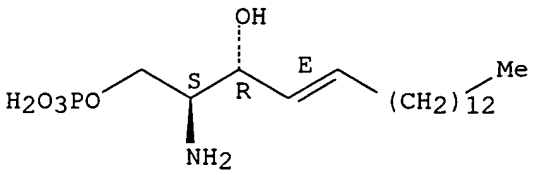
the nature of the response dependent upon the cell type, concentration of test agent and the time period of incubation. RT-PCR studies revealed that edg-1,2,4,5 receptors are present in the primary normal osteoblastic cells, the MG63 and G292 cells. Only the G292 cells expressed the **edg-3** receptor to any significant extent.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of sphingosine-1-phosphate and lysophosphatidic acid on human osteoblastic cells)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:132782 CAPLUS
DOCUMENT NUMBER: 144:429708
TITLE: Sphingosine 1-phosphate receptors mediate stimulatory and inhibitory signalings for expression of adhesion molecules in endothelial cells
AUTHOR(S): Kimura, Takao; Tomura, Hideaki; Mogi, Chihiro; Kuwabara, Atsushi; Ishiwara, Mitsuteru; Shibasawa, Kunihiko; Sato, Koichi; Ohwada, Susumu; Im, Doon-Soon; Kurose, Hitoshi; Ishizuka, Tamotsu; Murakami, Masami; Okajima, Fumikazu
CORPORATE SOURCE: Laboratory of Signal Transduction, Institute for Molecular and Cellular Regulation, Gunma University, 3-39-15 Showa-machi, Maebashi, 371-8512, Japan
SOURCE: Cellular Signalling (2006), 18(6), 841-850
CODEN: CESIEY; ISSN: 0898-6568
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sphingosine 1-phosphate (S1P) stimulates expression of vascular cell adhesion mol.-1 and intercellular adhesion mol.-1 in human umbilical vein endothelial cells. S1P-induced actions were associated with nuclear factor kappa-B activation and inhibited by pertussis toxin as well as by antisense oligonucleotides specific to S1P receptors, especially, S1P3. S1P also stimulated endothelial nitric oxide synthase (eNOS) and its activation was markedly inhibited by the antisense oligonucleotide for the S1P1 receptor rather than that for the S1P3 receptor. The dose-response curve of S1P to stimulate adhesion mol. expression was shifted to the left in the presence of the phosphatidylinositol 3-kinase inhibitor wortmannin and the NOS inhibitor Nω-nitro-L-arginine Me ester. NO donor S-nitroso-N-acetylpenicillamine inhibited S1P-induced adhesion mol. expression. Moreover, **tumor** necrosis factor-α-induced adhesion mol. expression was markedly inhibited by S1P in a manner sensitive to inhibitors for PI3-K and NOS. These results suggest that S1P receptors are coupled to both stimulatory and inhibitory pathways for adhesion mol. expression. The stimulatory pathway involves nuclear factor

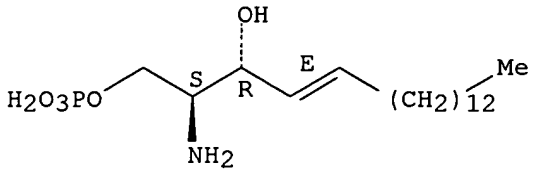
kappa-B and inhibitory one does phosphatidylinositol 3-kinase and NOS.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine 1-phosphate stimulated VCAM-1 and ICAM-1 expression through SIP3 receptor and NF-κB-involving pathway and SIP receptor coupled to inhibitory pathway involving PI3-K and NOS against adhesion mol. expression in HUVEC)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:287092 CAPLUS
DOCUMENT NUMBER: 136:384733
TITLE: Sphingosine 1-phosphate induces chemotaxis of immature dendritic cells and modulates cytokine-release in mature human dendritic cells for emergence of Th2 immune responses
AUTHOR(S): Idzko, Marco; Panther, Elisabeth; Corinti, Silvia; Morelli, Anna; Ferrari, Davide; Herouy, Yared; Dichmann, Stefan; Mockenhaup, Maja; Gebicke-Haerter, Peter; Di Virgilio, Francesco; Girolomoni, Giampiero; Norgauer, Johannes
CORPORATE SOURCE: Department of Experimental Dermatology, Freiburg, Germany
SOURCE: FASEB Journal (2002), 16(6), 625-627, 10.1096/fj.01-0625fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sphingosine 1-phosphate (S1P) is a potent extracellular lysolipid phosphoric acid mediator that is released after IgE-stimulation of mast cells. Here we investigated the biol. activity and intracellular signaling of S1P on human dendritic cells (DC), which are specialized antigen presenting cells with the ability to migrate into peripheral tissues and lymph nodes, as well as control the activation of naive T cells. We show that immature and mature DC express the mRNA for different S1P receptors, such as endothelial differentiation gene (EDG)-1, **EDG-3**, EDG-5, and EDG-6. In immature DC, S1P stimulated pertussis toxin-sensitive Ca2+ increase actin-polymerization and chemotaxis. These responses were lost by DC matured with lipopolysaccharide. In maturing DC, however, S1P inhibited the secretion of **tumor** necrosis factor-α and interleukin (IL)-12, whereas it enhanced secretion of IL-10. As a consequence, mature DC exposed to S1P showed a reduced and increased capacity to generate allogeneic Th1 and Th2 responses, resp. In summary, our study implicates that S1P might regulate the trafficking of DC and ultimately favor Th2 lymphocyte-dominated

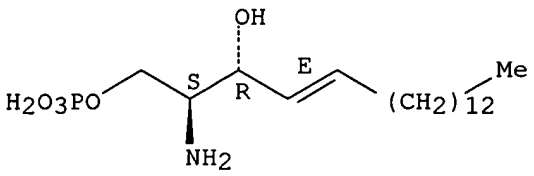
immunity.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine 1-phosphate induces chemotaxis of immature dendritic cells and modulates cytokine-release in mature human dendritic cells for emergence of Th2 immune responses)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:805366 CAPLUS

DOCUMENT NUMBER: 132:105964

TITLE: Sphingosine 1-phosphate stimulates cell migration through a Gi-coupled cell surface receptor. Potential involvement in angiogenesis

AUTHOR(S): Wang, Fang; Van Brocklyn, James R.; Hobson, John P.; Movafagh, Sharareh; Zukowska-Grojec, Zofia; Milstien, Sheldon; Spiegel, Sarah

CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Georgetown University Medical Center, Washington, DC, 20007, USA

SOURCE: Journal of Biological Chemistry (1999), 274(50), 35343-35350
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sphingosine 1-phosphate (SPP) has been shown to inhibit chemotaxis of a variety of cells, in some cases through intracellular actions, while in others through receptor-mediated effects. Surprisingly, the authors found that low concns. of SPP (10-100 nM) increased chemotaxis of HEK293 cells overexpressing the G protein-coupled SPP receptor EDG-1. In agreement with previous findings in human breast **cancer** cells, SPP, at micromolar concns., inhibited chemotaxis of both vector- and EDG-1-overexpressing HEK293 cells. Nanomolar concns. of SPP also induced a marked increase in chemotaxis of human umbilical vein endothelial cells (HUVEC) and bovine aortic endothelial cells (BAEC), which express the SPP receptors EDG-1 and **EDG-3**, while higher concns. of SPP were less effective. Treatment with pertussis toxin, which ADP-ribosylates and inactivates Gi-coupled receptors, blocked SPP-induced chemotaxis. Checkerboard anal. indicated that SPP stimulates both chemotaxis and chemokinesis. Taken together, these data suggest that SPP stimulates cell migration by binding to EDG-1. Similar to SPP, sphinganine 1-phosphate (dihydro-SPP), which also binds to this family of SPP receptors, enhanced chemotaxis, whereas, another structurally related lysophospholipid, lysophosphatidic acid, did not compete with SPP for binding nor did it have significant effects on chemotaxis of endothelial

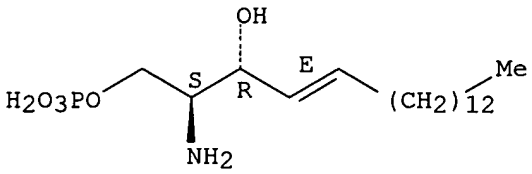
cells. Furthermore, SPP increased proliferation of HUVEC and BAEC in a pertussis toxin-sensitive manner. SPP and dihydro-SPP also stimulated tube formation of BAEC grown on collagen gels (in vitro angiogenesis), and potentiated tube formation induced by basic fibroblast growth factor. Pertussis toxin treatment blocked SPP-, but not bFGF-stimulated in vitro angiogenesis. These results suggest that SPP may play a role in angiogenesis through binding to endothelial cell Gi-coupled SPP receptors.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine 1-phosphate stimulation of cell migration through Gi-coupled cell surface receptor)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:355889 CAPLUS

DOCUMENT NUMBER: 142:408241

TITLE: Sphingosine 1-phosphate inhibits migration and RANTES production in human bronchial smooth muscle cells

AUTHOR(S): Kawata, Tadayoshi; Ishizuka, Tamotsu; Tomura, Hideaki; Hisada, Takeshi; Dobashi, Kunio; Tsukagoshi, Hideo; Ishiwara, Mitsuteru; Kurose, Hitoshi; Mori, Masatomo; Okajima, Fumikazu

CORPORATE SOURCE: Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, 3-39-15, Showa-machi, Maebashi, 371-8511, Japan

SOURCE: Biochemical and Biophysical Research Communications (2005), 331(2), 640-647
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sphingosine 1-phosphate (S1P), a bioactive lipid mediator, has been shown to be increased in bronchoalveolar lavage fluid after allergen challenge in asthmatic patients. Here, we examined S1P actions and their intracellular signalings in cultured human bronchial smooth muscle cells (BSMCs). Expression of mRNAs of three subtypes of S1P receptors, including S1P1, S1P2, and S1P3, was detected in BSMCs, and exposure of the cells to S1P inhibited platelet-derived growth factor (PDGF)-induced migration and **tumor** necrosis factor-α-induced RANTES production S1P also inhibited PDGF-induced Rac1 activation, and dominant neg. Rac1 inhibited PDGF-induced migration. On the other hand, dominant neg. Gαq attenuated the S1P-induced inhibition of RANTES production Finally, an S1P2-selective antagonist, JTE-013, suppressed the S1P-induced inhibition of migration response and RANTES production These results suggest that S1P attenuates cell migration by inhibiting a Rac1-dependent signaling pathway and decreases RANTES production by stimulating a

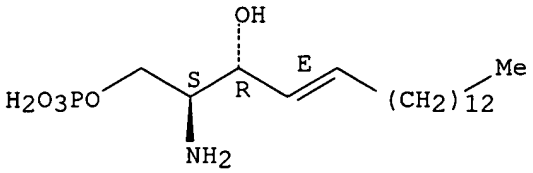
Gαq-dependent mechanism both possibly through the S1P2 receptors.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine 1-phosphate inhibits PDGF-induced migration through Rac1-dependent mechanism and decreases TNFα-induced RANTES production through Gαq-dependent mechanism in human bronchial smooth muscle cells)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:358266 CAPLUS

DOCUMENT NUMBER: 137:229795

TITLE: Sphingosine-1-phosphate stimulates human glioma cell proliferation through Gi-coupled receptors: role of ERK MAP kinase and phosphatidylinositol 3-kinase β

AUTHOR(S): Van Brocklyn, James R.; Letterle, Catherine A.; Snyder, Pamela J.; Prior, Thomas W.

CORPORATE SOURCE: Department of Pathology, The Ohio State University, Columbus, OH, 43210, USA

SOURCE: Cancer Letters (Shannon, Ireland) (2002), 181(2), 195-204
CODEN: CALEDQ; ISSN: 0304-3835

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

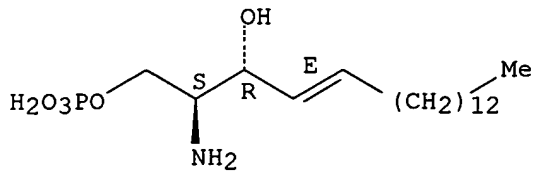
AB The regulation of glioma cell proliferation by sphingosine 1-phosphate (S1P) was studied using human glioblastoma cell line U-373 MG. The U-373 MG cells responded mitogenically to nanomolar concns. of S1P, and expressed mRNA encoding the S1P receptors S1P1/endothelial differentiation gene (EDG)-1, S1P3/**EDG-3**, and S1P2/EDG-5. S1P-induced proliferation required ERK kinase activation and was partially sensitive to pertussis toxin and wortmannin, indicating involvement of a Gi-coupled receptor and phosphatidylinositol 3-kinase. Moreover, S1P1, S1P3 and S1P2 receptors were expressed in the majority of human glioblastomas as determined by reverse transcriptase-polymerase chain reaction anal. Thus, S1P signaling through EDG receptors may contribute to glioblastoma growth in vivo.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of ERK2 kinase and phosphatidylinositol 3-kinase-β in sphingosine 1-phosphate stimulation of human glioma cell proliferation through Gi-coupled receptors)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



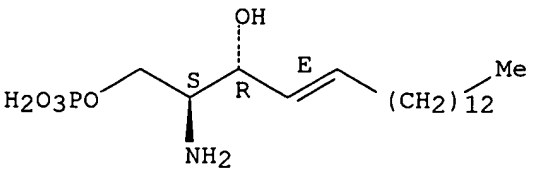
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:708612 CAPLUS
DOCUMENT NUMBER: 140:143536
TITLE: Sphingosine-1-phosphate stimulates motility and invasiveness of human glioblastoma multiforme cells
AUTHOR(S): Van Brocklyn, James R.; Young, Nicholas; Roof, Rosemary
CORPORATE SOURCE: Department of Pathology, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Cancer Letters (Oxford, United Kingdom) (2003), 199(1), 53-60
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sphingosine-1-phosphate (S1P) is a bioactive lipid which is a potent mitogen for glioblastoma multiforme cells. Here we show that S1P also potently enhances the in vitro motility of glioblastoma cells by signaling through receptors coupled to Gi/o proteins. Moreover, S1P also enhanced in vitro invasion of glioblastoma cells through Matrigel. S1P had no effect on matrix metalloproteinase secretion but did enhance glioblastoma cell adhesion. S1P is present at high levels in brain tissue. Thus it is possible that autocrine or paracrine signaling by S1P through its G protein-coupled receptors enhances both glioma cell proliferation and invasiveness.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(sphingosine-1-phosphate stimulates motility and invasiveness of human glioblastoma multiforme cells)
RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:605527 CAPLUS
DOCUMENT NUMBER: 145:62766
TITLE: Preparation of azetidinecarboxylic acid derivatives and β-alanine derivatives having ability of binding to sphingosine-1-phosphate (S1P) receptor
INVENTOR(S): Habashita, Hiromu; Kurata, Haruto; Nakade, Shinji
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

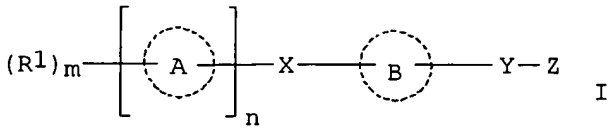
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006064757	A1	20060622	WO 2005-JP22765	20051212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

JP 2004-360539	A	20041213
JP 2005-125740	A	20050422
JP 2005-233790	A	20050811

GI



I

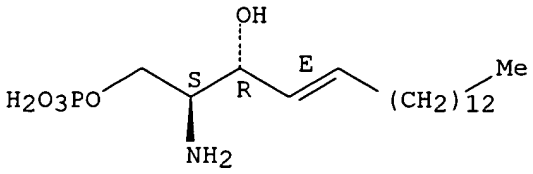
AB Aminocarboxylic acid derivs. represented by general formula (I), salts thereof, N-oxides thereof, solvates thereof, or prodrugs of any of these [ring A = cyclic group; ring B = (un)substituted cyclic group; X = a bond, a spacer having 1-8 atom(s) in the principal chain wherein one of the spacer atoms optionally forms an (un)substituted ring together with a substituent of the ring B; Y = a bond, a spacer having 1-10 atom(s) in the principal chain wherein one of the spacer atoms optionally forms an (un)substituted ring together with a substituent of the ring B; Z = (un)protected acidic group; n = 0 or 1, provided that when n is 0, m represent 1 and when R1 is H or a substituent and n is 1, m represents 0 or an integer of 1-7; R1 = a substituent] are prepared These compds. have the ability to bind with an S1P receptor (especially EDG-1, EDG-6, and/or EDG-8) and are agonists of EDG-1, EDG-6, and/or EDG-8. They are useful as immunosuppressants and/or for a method for decreasing lymphocyte and thereby for the prevention and/or treatment of diseases related to EDG-1, EDG-6, and/or EDG-8 which include rejection reactions to transplantation, graft vs. host diseases, autoimmune diseases, allergic diseases, neurodegenerative diseases, etc. Thus, 4.33 mL Et3N, 4.71 g Me azetidine-3-carboxylate hydrochloride, and 9.88 g sodium

triacetoxyborohydride were successively added to a solution of 5.04 g 6-[3-(4-fluorophenyl)propoxy]-1-methyl-3,4-dihydronaphthalene-2-carboxaldehyde in 50 mL THF and the resulting mixture was stirred at room temperature for 2.5 h to give, after workup and silica gel chromatog., 6.12 g Me
1-[[6-[3-(4-fluorophenyl)propoxy]-1-methyl-3,4-dihydro-2-naphthalenyl]methyl]-3-azetidinecarboxylate. In an EDG-1 agonist assay, 1-[[1-chloro-6-[(2-methoxy-4-propylbenzyl)oxy]-3,4-dihydro-2-naphthalenyl]methyl]-3-azetidinecarboxylic acid showed EC50 of 0.7 nmol/L for increasing the cellular Ca2+ ion concentration in CHO cells expressing EDG-1.
A tablet and ampule formulation-containing 1-[[1-chloro-6-(3-cyclohexylpropoxy)-3,4-dihydronaphthalen-2-yl]methyl]azetidine-3-carboxylic acid were prepared

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor agonists; preparation of azetidinecarboxylic acid derivs. and β-alanine derivs. having ability of binding to sphingosine-1-phosphate (S1P) receptor)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:558560 CAPLUS
DOCUMENT NUMBER: 145:40304
TITLE: Aryl amide sphingosine 1-phosphate analogs as S1P1/S1P3 receptor antagonists, and their therapeutic use
INVENTOR(S): Lynch, Kevin R.; MacDonald, Timothy L.; Clemens, Jeremy J.; Davis, Michael D.
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006063033	A2	20060615	WO 2005-US44231	20051206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-633587P P 20041206

OTHER SOURCE(S): MARPAT 145:40304

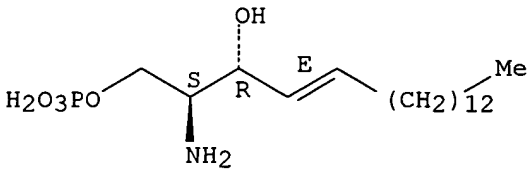
AB The invention provides compds. that have antagonist activity at the S1P1 and/or S1P3 receptors. These compds. have enhanced selectivity and potency at the S1P1 and/or S1P3 receptors. Preparation of the S1P analogs of the invention is described.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(aryl amide sphingosine 1-phosphate analogs as S1P1/S1P3 receptor antagonists, and therapeutic use)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L31 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:470641 CAPLUS

DOCUMENT NUMBER: 143:264174

TITLE: S1P2G protein-coupled receptor negatively regulates Rac, cell migration, chemoinvasion and experimental metastasis

AUTHOR(S): Takuwa, Noriko

CORPORATE SOURCE: Graduate School of Medicine, Kanazawa University, Japan

SOURCE: Kanazawa Daigaku Juzen Igakkai Zasshi (2004), 113(3-4), 93-97
CODEN: JUZIAG; ISSN: 0022-7226

PUBLISHER: Juzen Igakkai

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

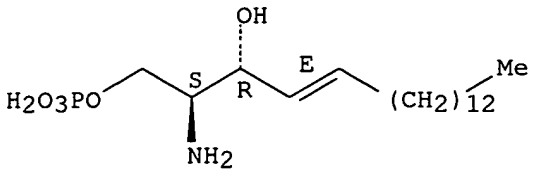
AB A review. The topics discussed are (1) G-protein coupled sphingosine-1-phosphate (S1P) receptor mediated Rac signal pathways and S1P2 in the suppression of Rac; (2) G12/13-coupled S1P2 in the suppression of Rac-induced chemoinvasion; (3) G12/13-coupled S1P3 and S1P2 signal pathways; (4) S1P receptors in the metastasis of melanoma B16 cells; and (5) roles of S1P receptors in cell migration and gene expression in blood vessel.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(G protein-coupled sphingosine-1-phosphate receptors in regulation of Rac, cell migration, invasion and metastasis)

RN 26993-30-6 CAPLUS

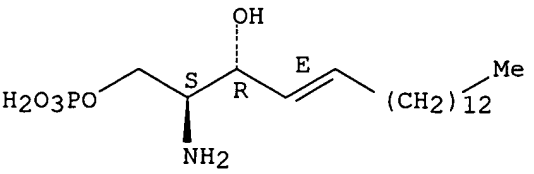
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L31 ANSWER 28 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:439193 CAPLUS
DOCUMENT NUMBER: 143:264158
TITLE: S1P2 G protein-coupled receptor negatively regulates Rac, cell migration, chemoinvasion and experimental metastasis
AUTHOR(S): Takuwa, Noriko; Sugimoto, Naotoshi; Takuwa, Yoh
CORPORATE SOURCE: Department of Molecular and Vascular Physiology, Graduate School of Medicine, Kanazawa University, Japan
SOURCE: Jikken Igaku (2005), 23(6, Zokan), 1014-1019
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. The topics discussed are (1) regulation of cell migration by G-protein coupled sphingosine-1-phosphate (S1P) receptors S1P1, S1P2 and S1P3; (2) G12/13-coupled S1P2 induced cell migration through Rho-mediated Rac activation; (3) G12/13-coupled S1P2 and S1P3 pathways; (4) regulation of melanoma B16 metastasis by S1P2; and (4) role of S1P receptors in blood vessels.
IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(G protein-coupled S1P2 receptor in neg. regulation of Rac, cell migration and metastasis)
RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L31 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:991667 CAPLUS
DOCUMENT NUMBER: 140:35986
TITLE: Methods of regulating differentiation in stem cells
INVENTOR(S): Pebay, Alice Marie; Pera, Martin Frederick
PATENT ASSIGNEE(S): ES Cell International Pte. Ltd., Australia
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003104442	A1	20031218	WO 2003-AU713		20030606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2488425	AA	20031218	CA 2003-2488425		20030606
AU 2003229140	A1	20031222	AU 2003-229140		20030606
EP 1511838	A1	20050309	EP 2003-724670		20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
GB 2405642	A1	20050309	GB 2004-28150		20030606
JP 2006505248	T2	20060216	JP 2004-511502		20030606
US 2004214319	A1	20041028	US 2003-657703		20030909
US 2005266553	A1	20051201	US 2004-6300		20041207
PRIORITY APPLN. INFO.:			AU 2002-2860	A	20020607
			AU 2002-2861	A	20020607
			AU 2003-901313	A	20030321
			AU 2003-902729	A	20030602
			WO 2003-AU713	W	20030606

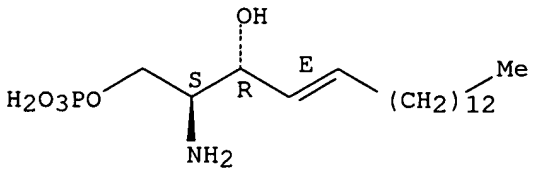
AB The present invention provides methods, media and compns. capable of modulating the differentiation of stem cells. Applicants have discovered that agonists of lysophospholipid receptors and ligands of class III tyrosine kinase receptors are useful in preventing the spontaneous differentiation of stem cells. The ligands and agonists may be used alone, or in combination where they have a synergistic effect. Also provided are cells produced using the methods and media, and methods of treating stem cell related diseases using the compns. described herein. Methods of identifying compds. useful in finding other agents useful in the modulation of stem cell differentiation are also disclosed.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulating differentiation in stem cells using lysophospholipid receptor agonists and class III tyrosine kinase receptor ligands for undifferentiated stem cell culture and treatment of differentiation disorders)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



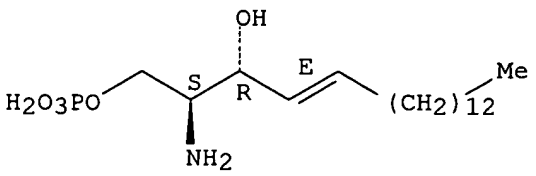
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:967491 CAPLUS
DOCUMENT NUMBER: 140:267976
TITLE: Microglial activation state and lysophospholipid acid receptor expression
AUTHOR(S): Tham, Chui-Se; Lin, Fen-Fen; Rao, Tadimeti S.; Yu, Naichen; Webb, Michael
CORPORATE SOURCE: Molecular Neuroscience Laboratory, Merck Research Laboratories, San Diego, CA, 92121, USA
SOURCE: International Journal of Developmental Neuroscience (2003), 21(8), 431-443
CODEN: IJDND6; ISSN: 0736-5748
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We used a simple com. magnetic immunobead method for the preparation of acutely isolated microglial cells from postnatal days 1-3 rat brain. With the exception of a 15 min enzyme incubation, all stages are carried out at 4°, minimizing the opportunity for changes in gene expression during the isolation to be reflected in changes in accumulated mRNA. The composition of the isolated cells was compared with that of microglial cultures prepared by conventional tissue culture methods, and the purity of microglia was comparable between the two prepns. RT-PCR anal. of several genes related to inflammatory products indicated that the acutely prepared cells were in a less activated condition than the conventionally tissue cultured cells. We examined the pattern of expression of receptors for lysophosphatidic acid (lpa) and sphingosine-1-phosphate (S1P) using quant. real-time PCR (TaqMan PCR) techniques. MRNA for LPA1, S1P1, S1P2, S1P3 and S1P5 was detected in these prepns., but the levels of the different receptor mRNAs varied according to the state of activation of the cells. MRNA for LPA3 was only detected significantly in cultured cell after lipopolysaccharide (LPS) stimulation, being almost absent in cultured microglia and undetectable in the acutely isolated prepns. The levels of mRNA of LPA1 and S1P receptors was reduced by overnight exposure to S1P, while the same treatment significantly up-regulated the level of LPA3 mRNA.

IT **26993-30-6**, Sphingosine-1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(microglial activation state and lysophospholipid acid receptor expression)
RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:587551 CAPLUS
DOCUMENT NUMBER: 135:302740
TITLE: Sphingosine 1-phosphate modulates human airway smooth

muscle cell functions that promote inflammation and airway remodeling in asthma

AUTHOR(S): Ammit, Alaina J.; Hastie, Annette T.; Edsall, Lisa C.; Hoffman, Rebecca K.; Amrani, Yassine; Krymskaya, Vera P.; Kane, Sibyl A.; Peters, Stephen P.; Penn, Raymond B.; Spiegel, Sarah; Panettieri, Reynold A., Jr.

CORPORATE SOURCE: Pulmonary, Allergy and Critical Care Division, Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA

SOURCE: FASEB Journal (2001), 15(7), 1212-1214, 10.1096/fj.00-0742fje
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

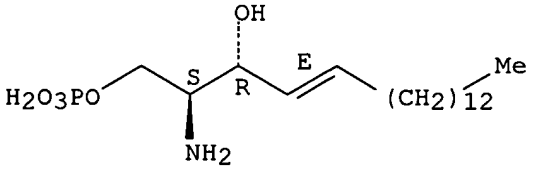
AB Asthma is characterized by airway inflammation, remodeling, and hyperresponsiveness to contractile stimuli that promote airway constriction and wheezing. Here we present evidence that sphingosine 1-phosphate (SPP) is a potentially important inflammatory mediator implicated in the pathogenesis of airway inflammation and asthma. SPP levels were elevated in the airways of asthmatic (but not control) subjects following segmental antigen challenge, and this increase was correlated with a concomitant increase in airway inflammation. Because human airway smooth muscle (ASM) cells expressed EDG receptors for SPP (EDG-1, -3, -5, and -6), we examined whether SPP may play a role in airway inflammation and remodeling, by affecting ASM cell growth, contraction, and cytokine secretion. SPP is mitogenic and augments EGF- and thrombin-induced DNA proliferation by increasing G1/S progression. SPP increased phosphoinositide turnover and intracellular calcium mobilization, the acute signaling events that affect ASM contraction. By modulating adenylate cyclase activity and cAMP accumulation, SPP had potent effects on cytokine secretion. Although SPP inhibited TNF-α-induced RANTES release, it induced substantial IL-6 secretion alone and augmented production of IL-6 induced by TNF-α. These studies are the first to associate SPP with airway inflammation and to identify SPP as an effective regulator of ASM growth, contraction and synthetic functions.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(sphingosine 1-phosphate in EDG receptor-mediated modulating human airway smooth muscle cell growth, contraction and cAMP-dependent cytokine secretion promoting inflammation and airway remodeling in asthma)

RN 26993-30-6 CAPLUS

CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

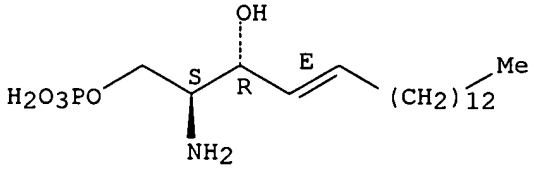
L31 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:342306 CAPLUS
DOCUMENT NUMBER: 140:389134
TITLE: Membrane type 1-matrix metalloproteinase (MT1-MMP) cooperates with sphingosine 1-phosphate to induce endothelial cell migration and morphogenic differentiation
AUTHOR(S): Langlois, Stephanie; Gingras, Denis; Beliveau, Richard
CORPORATE SOURCE: Laboratoire de Medecine Moleculaire Ste-Justine-Universite du Quebec a Montreal, Centre de Cancerologie Charles-Bruneau, Hopital Ste-Justine et Universite du Quebec a Montreal, Montreal, QC, Can.
SOURCE: Blood (2004), 103(8), 3020-3028
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Membrane type 1-matrix metalloproteinase (MT1-MMP) has been suggested to play an important role in angiogenesis, but the mechanisms involved remain incompletely understood. Using an in vitro model of angiogenesis in which cell migration of bovine aortic endothelial cells (BAECs) and their morphogenic differentiation into capillary-like structures on Matrigel are induced by overexpression of MT1-MMP, we show that the platelet-derived bioactive lipid sphingosine 1-phosphate (S1P) is the predominant serum factor essential for MT1-MMP-dependent migration and morphogenic differentiation activities. In the presence of S1P, MT1-MMP-dependent cell migration and morphogenic differentiation were inhibited by pertussis toxin, suggesting the involvement of Gi-protein-coupled receptor-mediated signaling. Accordingly, cotransfection of BAECs with MT1-MMP and a constitutively active Gαi2 (Q205L) mutant increased cell migration and morphogenic differentiation, whereas treatment of BAECs overexpressing MT1-MMP with antisense oligonucleotides directed against S1P1 and S1P3, the predominant S1P receptors, significantly inhibited both processes. These results demonstrate that MT1-MMP-induced migration and morphogenic differentiation involve the cooperation of the enzyme with platelet-derived bioactive lipids through S1P-mediated activation of Gαi-coupled S1P1 and S1P3 receptors. Given the important contribution of platelets to **tumor** angiogenesis, the stimulation of endothelial MT1-MMP function by S1P may thus constitute an important mol. event linking hemostasis to angiogenesis.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(MT1-MMP cooperates with sphingosine 1-phosphate to induce endothelial cell migration and morphogenic differentiation through S1P-mediated activation of Gαi-coupled S1P1 and S1P3 receptors)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

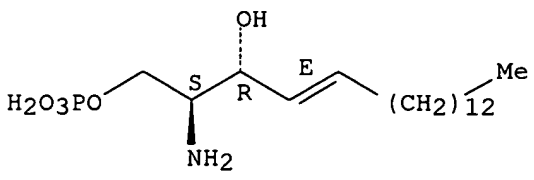
L31 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1094955 CAPLUS
DOCUMENT NUMBER: 144:3967
TITLE: Regulation of sphingosine 1-phosphate-induced endothelial cytoskeletal rearrangement and barrier enhancement by S1P1 receptor, PI3 kinase, Tiam1/Rac1, and α-actinin
AUTHOR(S): Singleton, Patrick A.; Dudek, Steven M.; Chiang, Eddie T.; Garcia, Joe G. N.
CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, Center for Translational Respiratory Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA
SOURCE: FASEB Journal (2005), 19(12), 1646-1656, 10.1096/fj.05-3928com
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Endothelial cell (EC) barrier dysfunction results in increased vascular permeability observed in inflammation, **tumor** angiogenesis, and atherosclerosis. The platelet-derived phospholipid sphingosine-1-phosphate (S1P) decreases EC permeability in vitro and in vivo and thus has obvious therapeutic potential. We examined S1P-mediated human pulmonary artery EC signaling and barrier regulation in caveolin-enriched microdomains (CEM). Immunoblotting from S1P-treated EC revealed S1P-mediated rapid recruitment (1 μM, 5 min) to CEMs of the S1P receptors S1P1 and S1P3, p110 PI3 kinase α and β catalytic subunits, the Rac1 GEF, Tiam1, and α-actinin isoforms 1 and 4. Immunopptd. p110 PI3 kinase catalytic subunits from S1P-treated EC exhibited PIP3 production in CEMs. Immunopptn. of S1P receptors from CEM fractions revealed complexes containing Tiam1 and S1P1. PI3 kinase inhibition (LY294002) attenuated S1P-induced Tiam1 association with S1P1, Tiam1/Rac1 activation, α-actinin-1/4 recruitment, and EC barrier enhancement. Silencing of either S1P, or Tiam1 expression resulted in the loss of S1P-mediated Rac1 activation and α-actinin-1/4 recruitment to CEM. Finally, silencing S1P1, Tiam1, or both α-actinin isoforms 1/4 inhibits S1P-induced cortical F-actin rearrangement and S1P-mediated barrier enhancement. Taken together, these results suggest that S1P-induced recruitment of S1P, to CEM fractions promotes PI3 kinase-mediated Tiam1/Rac1 activation required for α-actinin-1/4-regulated cortical actin rearrangement and EC barrier enhancement.

IT **26993-30-6**, Sphingosine 1-phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(regulation of sphingosine 1-phosphate-induced endothelial cytoskeletal rearrangement and barrier enhancement by S1P1 receptor, PI3 kinase, Tiam1/Rac1, and α-actinin)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:171669 CAPLUS
DOCUMENT NUMBER: 136:210572
TITLE: Method for regulating angiogenesis
INVENTOR(S): Hla, Timothy; Lee, Meng-jer; Claffey, Kevin P.; Ancellin, Nicolas; Thangada, Shobha
PATENT ASSIGNEE(S): University of Connecticut, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

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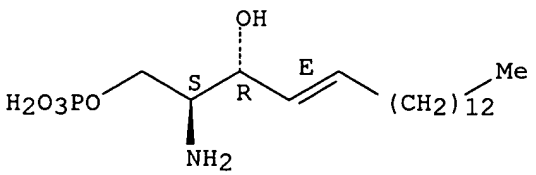
AB Methods for the inhibition of angiogenesis are presented, comprising affecting the response of the EDG-1 receptor by the administration of pharmaceutically effective antagonists of EDG-1 signal transduction. This invention is based in part on the discovery that Akt protein kinase phosphorylation is required for endothelial cell chemotaxis mediated by the EDG-1 G protein-coupled receptor. This invention relates to the use of modifiers of EDG-1 signal transduction to treat disorders of undesired angiogenesis.

IT **26993-30-6**, Sphingosine 1 phosphate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(EDG-1 receptor modulation method for regulating angiogenesis)

RN 26993-30-6 CAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, 1-(dihydrogen phosphate), (2S,3R,4E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



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L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
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RN 569655-99-8P
RN 569656-00-4P
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